Clinical Study Data Reviewer's Guide

sBLA Analysis for Participants, 12-15 Years of Age

BioNTech SE and PFIZER INC.

Study C4591001

Clinical Data Reviewer's Guide Revision history

Version	Summary of Major Change(s) and Impact	Version Date
1.0	First approved version of Clinical Data Reviewer's Guide	06-Dec-2021

Clinical Study Data Reviewer's Guide

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1. Introduction

1.1 Purpose

This document provides context for tabulation datasets and terminology that benefit from additional explanation beyond the Data Definitions document (define.xml). In addition, this document provides a summary of SDTM conformance findings.

1.2 Acronyms

Acronym	Translation
GMR	Geometric Mean Ratio
modRNA	Nucleoside-Modified Messenger Ribonucleic Acid
NAAT	Nucleic Acid Amplification Test
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SoA	Schedule of Activities
VE	Vaccine Efficacy
WOCBP	Woman/Women of Childbearing Potential

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	•SDTM v1.4 •SDTM-IG v3.2
Controlled Terminology	CDISC SDTM Controlled Terminology, 2020-03-27
Data Definitions	Define-XML v2.0

Standard or Dictionary	Versions Used
Medications Dictionary	WHODD GLOBALB3Mar21, SNOMED 2020-09-01, UNII 2020-08-18, MED-RT 2020-09-08
Medical Events Dictionary	MedDRA v24.0

2. Protocol Description

2.1 Protocol Number and Title

Protocol Number: C4591001

Protocol Short 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.

Note: Protocol Amendment's 13, 14 and beyond mentioned elsewhere in the submission documentation are out of scope for this submission and have not been included in this cSDRG.

Protocol Versions:

Amendment 12: 2021-01-14

- Because of a formatting error in protocol amendment 11, exclusion criterion 4 was inadvertently added to exclusion criterion 3 and the subsequent criteria renumbered. This amendment corrects that error.

Amendment 11: 2021-01-04

- Added a potential intensive surveillance period for nasal swabbing, for assessment via NAAT:
  - Corresponding SoA and procedures added

Amendment 10: 2020-12-01

- Added the possibility of administering BNT162b2 to participants who originally received placebo, following any local or national recommendations.
- Added the possibility of administering BNT162b2 to participants who originally received placebo, following completion of the active safety surveillance period.

Amendment 9: 2020-10-29

- To better align with the natural history of SARS-CoV-2 infection, added Phase 2/3 secondary efficacy objectives, estimands, and endpoints to include COVID-19 cases that occur from 14 days after the second dose; also modified the existing secondary efficacy objectives, estimands, and endpoints to include COVID-19 cases that occur from 14 days, as well as 7 days, after the second dose;
  - Made corresponding changes to the study design, study assessments and procedures, and statistical analysis sections.

- Clarified that interim analyses will be conducted after accrual of at least 62, 92, and 120 cases.
- Included any participants 16 through 17 years of age enrolled under this amendment in the reactogenicity subset.
- Clarified that serology data after a postbaseline positive SARS-CoV-2 test result will not be included in the analysis based on the evaluable immunogenicity populations.

Amendment 8: 2020-10-15

- Clarified that for participants who are not in the reactogenicity subset, local reactions and systemic events following vaccination should be detected and reported as AEs.
- Clarified that premenarchal females are not WOCBP.

Amendment 7: 2020-10-06

- Reduced the lower age range to include adolescents 12 to 15 years of age and added corresponding objectives.
- Added that 2 periods of potential COVID-19 symptoms within 4 days will be considered as a single illness.

Amendment 6: 2020-09-08

- Removed exclusion criterion 2 (ie, known infection with HIV, HCV, or HBV) for Phase 3 and added criteria for HIV-positive participants.
- Decreased the lower age limit and removed the upper age limit for inclusion in Phase 2/3 in order to evaluate BNT162b2 30 µg in older adolescents and those over 85 years of age; updated the title and other references to adults to align with this change.
- Clarified that inclusion criterion 4 (ie, participants at higher risk for acquiring COVID-19) is applicable for Phase 2/3 only, and provided some examples

Amendment 5: 2020-07-24

- Clarified that a single vaccine candidate, administered as 2 doses 21 days apart, will be studied in Phase 2/3.
- Stated that the vaccine candidate selected for Phase 2/3 evaluation is BNT162b2 at a dose of 30 µg.
- Renamed Stage 1 to Phase 1, removed Stage 2, and renamed Stage 3 to Phase 2/3.
- Clarified which stopping rules apply to which phase of the study.
- Moved the immunogenicity objectives in Phase 2/3 to become exploratory.
- Modified exclusion criterion 5, so that participants with a previous clinical or microbiological diagnosis of COVID-19 are excluded from all phases of the study.

Amendment 4: 2020-06-30

- BNT162b3 candidate has been added to the protocol.
- Further nonclinical data are available to support the study of the BNT162b3 candidate in humans, and the candidate has been added to the protocol.
- The 6-month safety follow-up telephone contact has been changed to an in-person visit for Stage 3 participants, to allow collection of an immunogenicity blood sample.

Amendment 3: 2020-06-10

- 20-µg dose level is formally included for BNT162b1 and BNT162b2.
- In order to increase flexibility enrolling participants, an extended screening window (increased from 14 to 28 days) for sentinel participants in Stage 1 has been added. This is

considered acceptable since eligible participants are expected to be either healthy or have stable medical conditions.

Amendment 2: 2020-05-27

- Added a 50-µg dose level for vaccine candidates based on the modRNA platform (ie, BNT162b1, BNT162b2, and BNT162b3).

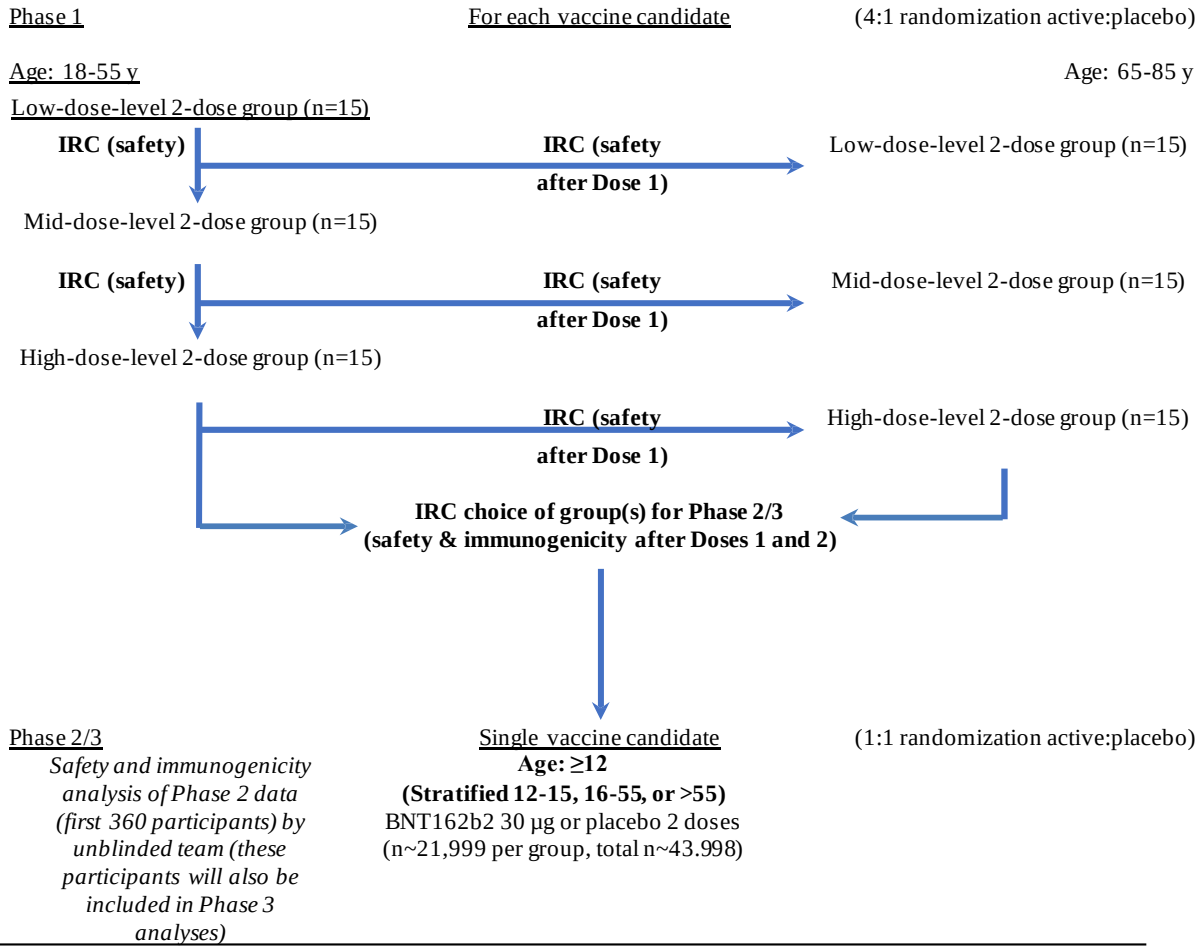
Amendment 1: 2020-05-13

- Decreased the dose levels for BNT162a1 and BNT162c2
- Modified exclusion criteria and prohibited inhaled/nebulized corticosteroids for sentinel participants in Stage 1.

Original Protocol 2020-04-15

2.2 Protocol Design

The study consists of 2 parts. Phase 1: to identify preferred vaccine candidate(s) and dose level(s); Phase 2/3: an expanded cohort and efficacy part. These parts, and the progression between them, are detailed in the schema.



Abbreviation: IRC = internal review committee.

The study will evaluate the safety, tolerability, and immunogenicity of 2 different SARS-CoV-2 RNA vaccine candidates against COVID-19 and the efficacy of 1 candidate:

- As a 2-dose (separated by 21 days) schedule;
- At various different dose levels in Phase 1;
- In 3 age groups: (Phase 1: 18 to 55 years of age, 65 to 85 years of age; Phase 2/3: ≥ 12 years of age [stratified as 12-15, 16-55, or >55 years of age]).

Dependent upon safety and/or immunogenicity data generated during the course of this study, or the BioNTech study conducted in Germany (BNT162-01), it is possible that groups in Phase 1 may be started at the next highest dose, groups may not be started, groups may be terminated early, and/or groups may be added with dose levels below the lowest stated dose or intermediate between the lowest and highest stated doses.

The study is observer-blinded, as the physical appearance of the investigational vaccine candidates and the placebo may differ. The participant, investigator, study coordinator, and other site staff will be blinded. At the study site, only the dispenser(s)/administrator(s) are unblinded.

To facilitate rapid review of data in real time, sponsor staff will be unblinded to vaccine allocation for the participants in Phase 1.

2.2.1 Phase 1

Each group (vaccine candidate/dose level/age group) will comprise 15 participants; 12 participants will be randomized to receive active vaccine and 3 to receive placebo.

For each vaccine candidate/dose level/age group, the following apply:

- Additional safety assessments (see protocol, Section 8.2)
- Controlled enrollment (required only for the first candidate and/or dose level studied):
  - No more than 5 participants (4 active, 1 placebo) can be vaccinated on the first day
  - The first 5 participants must be observed by blinded site staff for at least 4 hours after vaccination for any acute reactions
  - Vaccination of the remaining participants will commence no sooner than 24 hours after the fifth participant received his or her vaccination
- Application of stopping rules
- IRC review of safety data to determine escalation to the next dose level in the 18- to 55-year age cohort:
  - Escalation between dose levels will be based on IRC review of at least 7-day post–Dose 1 safety data in this study and/or the BioNTech study conducted in Germany (BNT162-01)

- Note that, since both candidates are based upon the same RNA platform, dose escalation for the second candidate studied may be based upon the safety profile of the first candidate studied being deemed acceptable at the same, or a higher, dose level by the IRC

Groups of participants 65 to 85 years of age will not be started until safety data for the RNA platform have been deemed acceptable at the same, or a higher, dose level in the 18- to 55-year age cohort by the IRC.

In this phase, 13 groups will be studied, corresponding to a total of 195 participants.

The IRC will select 1 vaccine candidate that, in Phase 1, has an established dose level per age group based on induction of a post–Dose 2 immune response, including neutralizing antibodies, which is expected to be associated with protection against COVID-19, for progression into Phase 2/3.

Participants who originally received placebo and become eligible for receipt of BNT162b2 or another COVID-19 vaccine according to local or national recommendations (detailed separately, and available in the electronic study reference portal) will have the opportunity to receive BNT162b2 as part of the study. The investigator will ensure the participant meets at least 1 of the recommendation criteria. Any Phase 1 placebo recipient who has not already been offered the opportunity to receive BNT162b2 will be given this opportunity at the approximate time participants in Phase 2/3 reach Visit 4. Any participant who originally received placebo but then goes on to receive BNT162b2 will move to a new visit schedule (Protocol Section 1.3.3).

2.2.2 Phase 2/3

On the basis of safety and/or immunogenicity data generated during the course of this study, and/or the BioNTech study conducted in Germany (BNT162-01), 1 vaccine candidate was selected to proceed into Phase 2/3. Participants in this phase will be ≥12 years of age, stratified as follows: 12 to 15 years, 16 to 55 years, or >55 years. The 12- to 15-year stratum will comprise up to approximately 2000 participants enrolled at selected investigational sites. It is intended that a minimum of 40% of participants will be in the >55-year stratum. Commencement of each age stratum will be based upon satisfactory post–Dose 2 safety and immunogenicity data from the 18- to 55-year and 65- to 85-year age groups in Phase 1, respectively. The vaccine candidate selected for Phase 2/3 evaluation is BNT162b2 at a dose of 30 μg.

Phase 2/3 is event-driven. Under the assumption of a true VE rate of ≥60%, after the second dose of investigational product, a target of 164 primary-endpoint cases of confirmed COVID-19 due to SARS-CoV-2 occurring at least 7 days following the second dose of the primary series of the candidate vaccine will be sufficient to provide 90% power to conclude true VE >30% with high probability. The total number of participants enrolled in Phase 2/3 may vary depending on the incidence of COVID-19 at the time of the enrollment, the true underlying VE, and a potential early stop for efficacy or futility.

Assuming a COVID-19 attack rate of 1.3% per year in the placebo group, accrual of 164 first primary-endpoint cases within 6 months, an estimated 20% non-evaluable rate, and 1:1 randomization, the BNT162b2 vaccine candidate selected for Phase 2/3 is expected to comprise approximately 21,999 vaccine recipients. This is the number of participants initially targeted for Phase 2/3 and may be adjusted based on advice from DMC analyses of case accumulation and the

percentage of participants who are seropositive at baseline. Dependent upon the evolution of the pandemic, it is possible that the COVID-19 attack rate may be much higher, in which case accrual would be expected to be more rapid, enabling the study's primary endpoint to be evaluated much sooner.

The first 360 participants enrolled (180 to active vaccine and 180 to placebo, stratified equally between 18 to 55 years and >55 to 85 years) will comprise the "Phase 2" portion. Safety data through 7 days after Dose 2 and immunogenicity data through 1 month after Dose 2 from these 360 participants will be analyzed by the unblinded statistical team, reviewed by the DMC, and submitted to appropriate regulatory authorities for review. Enrollment may continue during this period and these participants would be included in the efficacy evaluation in the "Phase 3" portion of the study.

In Phase 3, up to approximately 2000 participants, enrolled at selected sites, are anticipated to be 12 to 15 years of age. Noninferiority of immune response to prophylactic BNT162b2 in participants 12 to 15 years of age to response in participants 16 to 25 years of age will be assessed based on the GMR of SARS-CoV-2 neutralizing titers using a 1.5-fold margin. A sample size of 225 evaluable participants (or 280 vaccine recipients) per age group will provide a power of 90.8% to declare the noninferiority in terms of GMR (lower limit of 95% CI for GMR >0.67). A random sample of 280 participants from each of the 2 age groups (12 to 15 years and 16 to 25 years) will be selected as an immunogenicity subset for the noninferiority assessment.

The initial BNT162b2 was manufactured using "Process 1"; however, "Process 2" was developed to support an increased scale of manufacture. In the study, each lot of "Process 2"-manufactured BNT162b2 will be administered to approximately 250 participants 16 to 55 years of age. The safety and immunogenicity of prophylactic BNT162b2 in individuals 16 to 55 years of age vaccinated with "Process 1" and each lot of "Process 2" study intervention will be described. A random sample of 250 participants from those vaccinated with study intervention produced by manufacturing "Process 1" will be selected for this descriptive analysis.

Participants are expected to participate for up to a maximum of approximately 26 months. The duration of study follow-up may be shorter among participants enrolled in Phase 1 dosing arms that are not evaluated in Phase 2/3.

Participants ≥ 16 years of age who originally received placebo and become eligible for receipt of BNT162b2 or another COVID-19 vaccine according to local or national recommendations (detailed separately, and available in the electronic study reference portal) will have the opportunity to receive BNT162b2 as part of the study. The investigator will ensure the participant meets at least 1 of the recommendation criteria.

Any Phase 2/3 placebo recipient ≥16 years of age who has not already been offered the opportunity to receive BNT162b2 will be given this opportunity from 6 months after Vaccination 2 (at the time of the originally planned Visit 4).

Any participant who originally received placebo but then goes on to receive BNT162b2 will move to a new visit schedule (Protocol Section 1.3.3).

An intensive period of surveillance to evaluate the efficacy of BNT162b2 against asymptomatic SARS-CoV-2 infection may be conducted at selected sites among Phase 2/3 participants following approval of protocol amendment 11. After an initial in-person visit where a blood sample will be collected and a nasal (midturbinate) swab obtained, nasal (midturbinate) swabs will be obtained from consented participants every 2 weeks until Visit 4, or a sufficient number of cases of SARS-CoV-2 infection have accrued to evaluate this objective, whichever is sooner, per the SoA. The swabs will be tested at a central laboratory using NAAT to detect SARS-CoV-2. Participants who originally received placebo and become eligible for receipt of BNT162b2 according to local or national recommendations and then receive BNT162b2 as part of the study will not participate in surveillance for asymptomatic SARS-CoV-2 infection; if they become eligible during the surveillance period, the swabbing every 2 weeks will cease.

2.3 Trial Design Datasets

Are Trial Design datasets included in the submission? - **Yes**

Dataset	Dataset Label
TA	Trial Arms
TE	Trial Elements
TI	Trial Inclusion/Exclusion Criteria
TS	Trial Summary
TV	Trial Visits

2.3.1 TA - Trial Arms

For Phase 1, subjects were randomly assigned to receive either BNT162b1, BNT162b2, or placebo.

For Phase 2/3, subjects were randomly assigned to receive either BNT162b2 or placebo.

The detailed information for ARM and ARMCD was shown in the table below.

ARM	ARMCD
BNT162b1 Phase 1 (10 mcg)	B1_10
BNT162b1 Phase 1 (100/10 mcg)	B1_100
BNT162b1 Phase 1 (20 mcg)	B1_20
BNT162b1 Phase 1 (30 mcg)	B1_30
BNT162b2 Phase 1 (10 mcg)	B2_10
BNT162b2 Phase 1 (20 mcg)	B2_20
BNT162b2 Phase 1 (30 mcg)	B2_30
BNT162b2 Phase 2/3 (30 mcg)	B2_P23_30
Placebo	PLACEBO

2.3.2 TE - Trial Elements

There were ten trial elements in this study for Phase 1 including one screening element and eight vaccination elements: BNT162b1 (10 mcg), BNT162b1 (20 mcg), BNT162b1 (30 mcg), BNT162b1 (100 mcg), BNT162b2 (10 mcg), BNT162b2 (20 mcg), BNT162b2 (30 mcg), and Placebo. There was also one follow-up element.

There were 4 trial elements in this study for Phase 2/3 including one screening element and 2 vaccination elements: BNT162b2 (30 mcg) and Placebo. There was also one follow-up element.

For Placebo subject from Phase 1 that qualified to receive BNT162b2 (30 mcg), additional elements were included: Screening Open Label & Follow-up Open Label.

2.3.3 TI - Trial Inclusion/Exclusion Criteria

See Appendix I: Inclusion/Exclusion Criteria for the complete text of each inclusion or exclusion criteria.

2.3.4 TS - Trial Summary

The Trial Summary (TS) dataset details a summary of the trial in a structured format. Each record in the Trial Summary dataset contains the value of a parameter, a characteristic of the trial. Trial Summary was used to record basic information about the study such as trial phase, protocol title, and trial objectives, as well as information about the planned and actual trial characteristics.

In accordance with the FDA business rule, the values for PARAMCD equal to AGEMIN, PLANSUB, and NARMS has been combined into one record. The minimum age for Phase 1 is 18 years while Phase 2/3 is 12. The planned number of arms for Phase 1 is 7 while Phase 2/3 is 2.

2.3.5 TV - Trial Visits

The trial visits dataset describes the planned visits of the trial and consists of 19 visits for Phase 1 and 11 visits for Phase 2/3. Each visit and visit description are shown in the table below.

Visits V4_WEEK3_VAX2_S_R; V5_WEEK1_POSTVAX2_S_R; V6_WEEK2_POSTVAX2_S_R; V6_WEEK2_POSTVAX2_S_R; are for subjects who received 100mcg during vaccination 1 for Phase 1. Dose of 100 mcg was deemed too high and the dosing/visit was stopped for approximately 4

months. After 4 months, the subject returned and received 10 mcg at vaccination 2 and completed the rest of the visits.

Visits in the chart below with the suffix of "_S" and "_L" , excluding COVID visits, are related to Phase 1 and Phase 2/3 respectively.

VISITNUM	VISIT	VISITDY	Description
1	COVID_A		COVID-19 illness onset
200	COVID_A1		After the visit of COVID-19 illness onset
2	COVID_B		COVID-19 illness onset
201	COVID_B1		After the visit of COVID-19 illness onset
3	COVID_C		COVID-19 illness onset
202	COVID_C1		After the visit of COVID-19 illness onset
4	COVID_D		COVID-19 illness onset
203	COVID_D1		After the visit of COVID-19 illness onset
5	COVID_E		COVID-19 illness onset
204	COVID_E1		After the visit of COVID-19 illness onset
6	COVID_F		COVID-19 illness onset
205	COVID_F1		After the visit of COVID-19 illness onset
7	COVID_G		COVID-19 illness onset
206	COVID_G1		After the visit of COVID-19 illness onset
8	COVID_H		COVID-19 illness onset
207	COVID_H1		After the visit of COVID-19 illness onset
9	COVID_I		COVID-19 illness onset
208	COVID_I1		After the visit of COVID-19 illness onset
10	COVID_J		COVID-19 illness onset
209	COVID_J1		After the visit of COVID-19 illness onset
11	COVID_K		COVID-19 illness onset
210	COVID_K1		After the visit of COVID-19 illness onset
12	COVID_L		COVID-19 illness onset
211	COVID_L1		After the visit of COVID-19 illness onset
13	COVID_M		COVID-19 illness onset
212	COVID_M1		After the visit of COVID-19 illness onset
14	COVID_N		COVID-19 illness onset
213	COVID_N1		After the visit of COVID-19 illness onset
15	COVID_O		COVID-19 illness onset
214	COVID_O1		After the visit of COVID-19 illness onset
16	COVID_P		COVID-19 illness onset
215	COVID_P1		After the visit of COVID-19 illness onset
17	COVID_Q		COVID-19 illness onset
216	COVID_Q1		After the visit of COVID-19 illness onset
18	COVID_R		COVID-19 illness onset
217	COVID_R1		After the visit of COVID-19 illness onset
19	COVID_S		COVID-19 illness onset
218	COVID_S1		After the visit of COVID-19 illness onset

VISITNUM	VISIT	VISITDY	Description
20	COVID_T		COVID-19 illness onset
219	COVID_T1		After the visit of COVID-19 illness onset
60776	End of Treatment		Start of end of treatment visit
60777	Follow-Up		First day of follow-up visit
60772	POT_COVID_CONVA		28 to 35 days after potential COVID-19 illness visit
60771	POT_COVID_ILL		Optimally within 3 days after potential COVID-19 illness onset
51231792	REVAX_CONTACT		Start of contact
60747	SCR		Informed consent
20210	SSWAB_WEEK10		Surveillance swab sample collection at week 10
20212	SSWAB_WEEK12		Surveillance swab sample collection at week 12
20214	SSWAB_WEEK14		Surveillance swab sample collection at week 14
20216	SSWAB_WEEK16		Surveillance swab sample collection at week 16
20218	SSWAB_WEEK18		Surveillance swab sample collection at week 18
20202	SSWAB_WEEK2		Surveillance swab sample collection at week 2
20220	SSWAB_WEEK20		Surveillance swab sample collection at week 20
20222	SSWAB_WEEK22		Surveillance swab sample collection at week 22
20224	SSWAB_WEEK24		Surveillance swab sample collection at week 13
20226	SSWAB_WEEK26		Surveillance swab sample collection at week 14
20228	SSWAB_WEEK28		Surveillance swab sample collection at week 15
20204	SSWAB_WEEK4		Surveillance swab sample collection at week 4
20206	SSWAB_WEEK6		Surveillance swab sample collection at week 6
20208	SSWAB_WEEK8		Surveillance swab sample collection at week 8
60765	V1_DAY1_VAX1_L	1	Day 1
60748	V1_DAY1_VAX1_S	1	Day 1
60757	V10_MONTH24_S	749	714 to 742 days after visit 4
51231793	V101_VAX3		Open label vaccination 1
51231794	V102_VAX4		Open label vaccination 2
51231795	V103_MONTH1		28 to 35 Days after visit 102
51231796	V104_MONTH6		175 to 189 days after visit 102
51231797	V105_MONTH18		532 to 560 days after visit 102
60749	V2_DAY2_POSTVAX1_S	2	1 to 3 days after visit 1
60766	V2_VAX2_L	21	19 to 23 days after visit 1 or 56 to 70 days after visit
56985855	V201_SURVEIL_CONSENT		Infection Surveillance Consent
60767	V3_MONTH1_POSTVAX2_L	51	28 to 35 days after visit 2
60750	V3_WEEK1_POSTVAX1_S	7	6 to 8 days after visit 1
60768	V4_MONTH6_L	173	154 to 168 days after visit 2
60751	V4_WEEK3_VAX2_S	21	19 to 23 days after visit 1
1165454	V4_WEEK3_VAX2_S_R		NA
60769	V5_MONTH12_L	371	350 to 378 days after visit 2
60752	V5_WEEK1_POSTVAX2_S	28	6 to 8 days after visit 4
1165455	V5_WEEK1_POSTVAX2_S_R		6 to 8 days after visit 4_R
60770	V6_MONTH24_L	733	714 to 742 days after visit 2
60753	V6_WEEK2_POSTVAX2_S	35	12 to 16 days after visit 4

VISITNUM	VISIT	VISITDY	Description
1165456	V6_WEEK2_POSTVAX2_S_R		12 to 16 days after visit 4_R
60754	V7_MONTH1_S	52	28 to 35 days after visit 4
1165457	V7_MONTH1_S_R		28 to 35 days after visit 4_R
60755	V8_MONTH6_S	182	154 to 168 days after visit 4
60756	V9_MONTH12_S	385	350 to 378 days after visit 4

3. Subject Data Description

3.1 Overview

Are the submitted data taken from an ongoing study? **Yes**

For analysis, a data cutoff of 02Sept2021 was applied on the SDTM data. Furthermore, any data related to the booster portion of the Phase 1 subjects was also programmatically excluded from SDTM data. Details about the cutoff algorithm applied to the SDTM data can be found in Appendix II.

Were the SDTM datasets used as sources for the analysis datasets? **Yes**

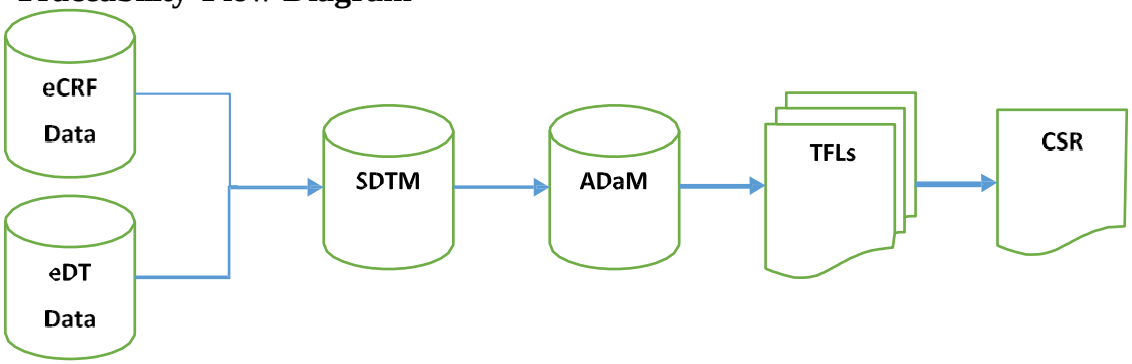
Do the submission datasets include screen failures? **No**

Were any domains planned, but not submitted because no data were collected? **No**

Are the submitted data a subset of collected data? **No**

Is adjudication data present? **No**

3.2 Traceability Flow Diagram



3.3 Annotated CRFs

Collected fields and pages that have not been tabulated have been annotated as "Not Submitted". Pfizer collects certain data elements to facilitate operational processes including data cleaning and dynamically creating additional forms in the electronic data capture system. All fields and pages that have been annotated as "Not Submitted" meet this criterion and are described below.

aCRF page Number(s)	Data Collection Field	Explanation of why [NOT SUBMITTED]
24, 91, 93	1. Lowest Level Term, 2. Lowest Level Term Code, 3. High Level Term, 4. High Level Term Code, 5. High Level Group Term, 6. High Level Group Term Code, 7. Primary System Organ Class 8. Primary System Organ Class Code	Not needed for analysis
14	Cohort Selection	Not needed for analysis. The whole page is annotated as NOT SUBMITTED.
35	Inform Enrollment	Not needed for analysis. The whole page is annotated as NOT SUBMITTED.
36	HIV Status	Not needed for analysis. The whole page is annotated as NOT SUBMITTED.
63	Casebook Signature Form	Not needed for analysis. The whole page is annotated as NOT SUBMITTED.
84	Further Vaccination Confirmation	Not needed for analysis. The whole page is annotated as NOT SUBMITTED.
89	Inform Screening	Not needed for analysis. The whole page is annotated as NOT SUBMITTED.
95, 96, 97	Stratification	Not needed for analysis. The whole page is annotated as NOT SUBMITTED.
98	Subject Status	Not needed for analysis. The whole page is annotated as NOT SUBMITTED.
105	Unplanned assessments	Not needed for analysis. The whole page is annotated as NOT SUBMITTED.
12, 15, 16, 24, 40, 41, 42, 70, 72, 76, 77, 82, 83, 91, 93, 106, 108, 110	Comparison Term	Not needed for analysis.
15, 16, 76, 110	Concomitant Medications Pre-specified	Not needed for analysis.
33	COVID-19 Surveillance Visit	Not needed for analysis.
18, 19, 20, 21	1. Follow-Up Contact Category 2. Was contact made? 3. If No, why? 4. Comments	Not needed for analysis.
30, 31, 32, 33, 34	Erroneous Visit	Not needed for analysis.
105	Contact Outcome	Not needed for analysis.

40	1. Category of Clinical Event 2. Was a diagnosis obtained for Potential COVID-19 Illness? (NO)	Not needed for analysis.
41, 42	Was a diagnosis obtained? (NO)	Not needed for analysis.
64, 65	Lab Sub-Panel	Not needed for analysis.
87, 90, 100	Sample Collected?	Not needed for analysis.
75, 87, 88, 90, 100	Sample ID	Not needed for analysis.
81	CISR Category	Not needed for analysis.
91, 93	Event Pre-specified	Not needed for analysis.
102	1. Were fever or systemic symptoms present on the last day the Subject Diary was completed? 2. Were injection site reactions present on the last day the Subject Diary was completed?	Not needed for analysis.
108	Container Number	Not needed for analysis.

3.4 SDTM Subject Domains

Dataset - Dataset Label	Efficacy	Safety	Other	SUPP--	Related Using RELREC
AE - Adverse Events		X		X	DS, CE
CE - Clinical Events		X		X	AE, FACE, VS
CM - Concomitant Medications		X		X	
CO - Comments			X		
DI - Device Identifiers			X		MB, LB
DM - Demographics			X	X	
DS - Disposition			X	X	AE
DV - Protocol Deviations			X	X	
EC - Exposure as Collected			X	X	
EX - Exposure			X	X	
FACE - Findings About Events or Interventions		X		X	CE
FAHO - Findings About Events or Interventions		X			HO

Dataset - Dataset Label	Efficacy	Safety	Other	SUPP--	Related Using RELREC
HO - Healthcare Encounters		X		X	FAHO
IE - Inclusion/Exclusion Criteria Not Met			X	X	
IS - Immunogenicity Specimen Assessment	X			X	
LB - Laboratory Test Results		X		X	DI
MB - Microbiology Specimen			X	X	DI
MH - Medical History			X	X	
MO - Morphology			X	X	
SE - Subject Elements			X		
SV - Subject Visits			X		
VS - Vital Signs		X		X	CE

3.4.1 AE - Adverse Events

Adverse events dataset consists of one record per adverse event per subject.

The entry of a "Y" for the serious adverse event variable, AESER, indicates the AE meets the criteria as serious per investigator report and the definition in the CRF guidance.

Adverse events, medication errors, newly diagnosed chronic medical conditions and reactogenicity are included in the AE dataset and distinguished by AECAT. To implement the CDISC Vaccines TAUG flat model, records of reactogenicity are added to AE domain from CE with AECAT= "REACTOGENICITY", when the duration of reactogenicity events go beyond the planned observation period. AECAT = "MEDICATION ERROR" represents AE as a result of a study medication error collected in SUPPAE.

A relationship has been defined in RELREC between the disposition event where DSDECOD= ADVERSE EVENT or DEATH and the adverse event leading to discontinuation. The observations are related by AESEQ and DSSEQ. A relationship has also been defined between the adverse events and clinical event summary records and are related by AELNKGRP and CELNKGRP.

QNAM	Description
AECMGIV	Concomitant Medication Given
AEMEFL	Medication Error Associated With AE
AEMERES	Is AE a Result of a Medication Error
AENDGIV	Was a Non-Drug Treatment given

QNAM	Description
AERELTXT	Event Due to Other Specify
AESUBJDC	Discontinued because of this AE
DICTVER	Dictionary Name and Version
LSTCGDTC	Date/Time of Last change

3.4.2 CE - Clinical Events

Clinical Events dataset consists of one record per event per subject.

Clinical Events implements Vaccines TAUG flat model for reactogenicity records, where it summarizes each symptom event per vaccination per subject. CECAT = "REACTOGENICITY". The corresponding daily assessments from the e-diary are in FACE.

Unplanned assessments occurring during the diary period will be utilized along with the e-diary data in creating the summary records in CE, even if the assessment was not required per protocol (no symptom reported or symptom was reported but not severe). The worst reported severity will be mapped for each symptom in the summary record and stop date will reflect the latest symptom date from the e-diary or unplanned assessment, or from Symptom Resolved Dates form if continued past the diary period.

Reactogenicity exclusions are as follows:

- If subject is not part of reactogenicity subset but has unplanned reactogenicity assessments (unplanned temp or unplanned assessment of local reaction/systemic event), or has unplanned assessments without any diary data, then these unplanned assessments were dropped from FACE/VS and summary CE records were not generated.
- If an unplanned assessment exists with an assessment date (CEDTC) falling after the stop date recorded on the Symptom Resolved Dates CRF, these records were dropped from FACE for that visit. Only data up through the stop date from Symptom Resolved Dates in the CRF were used to create the CE records.
- If a subject has diary data and their symptom did not occur during the diary period but was on the unplanned assessment after diary period, then the unplanned assessment was dropped (symptom must begin during diary period to be part of reactogenicity).
- If there were unplanned assessments after the diary period and the Symptom Resolved Dates form was present but did not have a stop date or 'ongoing' recorded for that symptom, then the unplanned assessments were dropped.

Potential COVID-19 illness from the ILLNESS DETAILS - POTENTIAL COVID-19 ILLNESS CRF is included with CECAT = "EFFICACY". The investigator's diagnosis is in CETERM. Subjects who progress to severe disease, as defined in the protocol, will have data entered on the ILLNESS DETAILS - SEVERE COVID-19 ILLNESS CRF which is reported in the CE domain with CECAT = 'SEVERE COVID-19 ILLNESS' and CESCAT (Subcategory) denoting whether there was significant acute renal, hepatic, or neurologic dysfunction.
As agreed with CBER, CE includes event records for "COVID-19 like illness" and "COVID-19 confirmed" in the CE domain for subjects who were assigned to a vaccination arm (DM.ARM is not "SCREEN FAILURE" or "NOT ASSIGNED") as follows:

- The "COVID-19 confirmed" events are based on the "Clinical disease endpoint case flag" (CDECASE) in SUPPDM.
- "COVID-19 like illness" is flagged "Y" when a subject has at least one pre-specified symptom. Please note that a subject may have more than one occurrence of "COVID-19 like illness" if symptoms presented during different illness visits, but only has one record for "COVID-19 confirmed" that has a visit associated when the case was assessed to be positive.
- When there is confirmed COVID-19, the assessment of each pre-specified symptom corresponding to that symptomatic period (i.e., corresponding COVID Illness visit) will additionally be included in the CE domain, with CESCAT = "SIGNS AND SYMPTOMS OF DISEASE".
- As start and stop dates were not collected for each symptom individually, CESTDTC and CEENDTC was not populated for each symptom but the date first symptom started and date last symptom resolved was mapped to CESTDTC and CEENDTC in the "COVID-19 like illness" and "COVID-19 confirmed" records.
- The individual symptoms have VISIT and collection date (CEDTC) populated from the relevant COVID Illness visit.
- Toxicity grade for a COVID-19 like illness is collected in the ILLNESS DETAILS - POTENTIAL COVID-19 ILLNESS CRF so CETOXGR is populated instead of CESEV in the "COVID-19 like illness" and "COVID-19 confirmed" records. It is not collected for each symptom individually.
- For COVID illness, CRF will collect toxicity grade as 0 for asymptomatic subjects. If an illness visit is performed for asymptomatic participant, toxicity grade will be reported as "0" while the participant is asymptomatic. If participant later experiences symptoms, the appropriate toxicity grade will be updated.

A relationship has been defined in RELREC been defined between the adverse events and clinical event summary records and are related by AELNKGRP and CELNKGRP. A relationship has also been defined between clinical event summary records and findings about records. The observations are related by CELNKGRP and FALNKGRP. A relationship has also been defined between clinical event summary records and temperature vital signs records using CELNKGRP and VSLNKGRP.

QNAM	Description
CEDRVFL	Derived Flag
CEEVAL	Evaluator
DICTVER	Dictionary Name and Version
ONGNXVIS	Reported Ongoing at Next Visit
RCENDTC	Reported Clinical Event End Date

QNAM = "CEDRVFL" is used to indicate that an entire record is derived.

3.4.3 CM - Concomitant Medications

Concomitant Medications dataset consists of one record per recorded medication occurrence or constant-dosing interval per subject.

QNAM	Description
CMCODE	Standardized Medication Code
DICTVER	Dictionary Name and Version

3.4.4 CO - Comments

Comments dataset consists of one record per comment per subject.

3.4.5 DI - Device Identifiers

Device identifiers dataset consists of one record per device identifier per device.

A relationship has been defined in RELREC between the device identifier records and the corresponding laboratory and microbiology records. The observations are related by SPDEVID.

3.4.6 DM - Demographics

Demographics dataset consists of one record per subject.

Specify Other Race and Ethnicity have been submitted in SUPPDM.

QNAM	Description
CDECASE	Clinical disease endpoint case flag
RACE1	Race1
RACE2	Race2
RACIALD	Racial Designation
REACTOFL	Reactogenicity Population Flag

As agreed with CBER, CDECASE qualifier in SUPPDM is populated for each subject from the ADaM primary endpoint case flag for the first primary efficacy endpoint, as defined in the protocol. This flag is derived based on ADSL and ADC19EF ADaM datasets.

3.4.7 DS - Disposition

Disposition dataset consists of one record per disposition status or protocol milestone per subject.

If Participants terminated early, the appropriate reason for discontinuation as per protocol are recorded in the End of Treatment (EOT) and Follow-up (FUP) visit Disposition pages.
DSPHASE in SUPPDS corresponds to the pages and can be used to link the records with multiple disposition per EPOCH.

A relationship has been defined in RELREC between the disposition event where DSDECOD= ADVERSE EVENT or DEATH and the adverse event leading to discontinuation. The observations are related by AESEQ and DSSEQ.

QNAM	Description
DSPHASE	Disposition Phase

3.4.8 DV - Protocol Deviations

Protocol Deviations dataset consists of one record per protocol deviation per subject

QNAM	Description
ACTSITE	Actual Site of Deviation Occurrence
CAPE	Confirmed Analysis Population Exclusion
DESGTOR	Visit Designator
DVTERM1	Protocol Deviation Term 1
SOURCE	Source of the data

3.4.9 EC - Exposure as Collected

Exposure as collected dataset consists of one record per protocol-specified study treatment, collected-dosing interval, per subject, per mood.

QNAM	Description
ECCD	Standardized Medication Code
ECDECOD	Standardized Medication Name
ECOBSV	Observed Post Dose For Specified Time
ECOBSVD	Details Of Subject Observation
ECOBSVT	Timeframe Subject Was Observed
ECTDV	Temporary Delay of Vaccination
FDDTC	Date of First Delay

3.4.10 EX - Exposure

Exposure dataset consists of one record per constant dosing interval per subject.

- Participants ≥ 16 years of age who originally received placebo and became eligible for receipt of BNT162b2 or another COVID-19 vaccine will have additional vaccination records.
- For subjects with temporary delay of vaccination without treatment information and vaccination date, data will not be used or retained in SDTM.

QNAM	Description
EXCD	Standardized Medication Code
EXDECOD	Standardized Medication Name
EXOBSV	Observed Post Dose For Specified Time
EXOBSVD	Details Of Subject Observation
EXOBSVT	Timeframe Subject Was Observed
EXTDV	Temporary Delay of Vaccination
FDDTC	Date of First Delay

3.4.11 FACE - Findings About Events or Interventions

Findings About dataset consists of one record per finding per object per time point per time point

reference per visit per subject.

FACE implements flat model for reactogenicity records, including e-diary and unplanned assessments of reactogenicity findings. Unplanned assessments are under FACAT = "REACTOGENICITY - UNPLANNED ASSESSMENT" while diary data has FACAT = "REACTOGENICITY". FASTAT = "NOT DONE" records are generated for any missed diary days and are flagged with FADRVFL = "Y".

Subjects not part of reactogenicity subset should not have any e-diary data, unplanned assessments or Symptom Resolved Dates form completed.

a. Programming does not generate any 'NOT DONE' records for these subjects. Any e-diary and Symptom Resolved Dates CRF data that was completed is dropped if subject is not part of reactogenicity subset.
b. Unplanned assessments without an e-diary will be dropped from reactogenicity datasets and would be counted only as an adverse event or COVID-19 symptom in the relevant domain.

Signs and symptoms of COVID-19 are included with FACAT = "EFFICACY".

A relationship has been defined in RELREC between clinical event summary records and findings about records. The observations are related by CELNKGRP and FALNKGRP.

QNAM	Description
CLTYP	Collection Type
FALANG	Language Version of Instrument

3.4.12 FAHO - Findings About Events or Interventions

Findings About dataset consists of one record per finding per object per time point per time point reference per visit per subject.

A relationship has been defined in RELREC been defined between healthcare encounter events and the corresponding findings about event records. The observations are related by HOLNKID and FALNKID.

3.4.13 HO - Healthcare Encounters

Healthcare Encounters dataset consists of one record per healthcare encounter per subject.

A relationship has been defined in RELREC been defined between healthcare encounter events and the corresponding findings about event records. The observations are related by HOLNKID and FALNKID.

QNAM	Description
HCUHSP	Hospitalized due to COVID-19 illness?
HCUICU	Been in ICU due to COVID-19 illness?
HCUIDIS	Disease Name

3.4.14 IE - Inclusion/Exclusion Criteria Not Met

Inclusion/Exclusion Criteria Not Met dataset consists of one record per inclusion/exclusion criterion not met per subject.

3.4.15 IS - Immunogenicity Specimen Assessment

Immunogenicity Specimen Assessment dataset consists of one record per test per visit per subject.

QNAM	Description
ETRKDOR	Data Origin

3.4.16 LB - Laboratory Test Results

Laboratory Test Results dataset consists of one record per analyte per planned time point number per time point reference per visit per subject.

A relationship has been defined in RELREC between the device identifier records and the corresponding laboratory records. The observations are related by SPDEVID.

QNAM	Description
LBSTTYPE	Standardized Unit
LBUNEVFL	Not Evaluable Flag

3.4.17 MB - Microbiology Specimen

Microbiology Specimen dataset consists of one record per microbiology specimen finding per time point per visit per subject.

SARS-CoV-2 test results from local labs will have MBCAT = "CONFIRMATION OF INFECTION" (as collected in the CRF) and central labs have MBCAT = "VIROLOGY".

A relationship has been defined in RELREC between the device identifier records and the corresponding microbiology records. The observations are related by SPDEVID.

QNAM	Description
ETRKDOR	Data Origin
TRADEOTH	Other Trade Name

3.4.18 MH - Medical History

Medical History dataset consists of one record per medical history event per subject.

QNAM	Description
DICTVER	Dictionary Name and Version

3.4.19 MO - Morphology

Morphology dataset consists of one record per Morphology finding per location per time point per visit per subject.

3.4.20 SE - Subject Elements

Subject Elements dataset consists of one record per actual element per subject.

3.4.21 SV - Subject Visits

Subject Visits dataset consists of one record per actual visit per subject.

3.4.22 VS - Vital Signs

Vital Signs dataset consists of one record per vital sign measurement per time point per visit per subject.

To implement the CDISC Vaccines TAUG flat model, temperature records from e-diary are mapped to VS domain with VSCAT= "REACTOGENICITY". Any unplanned temperature assessments by the investigator post vaccination are included with VSCAT = "REACTOGENICITY - UNPLANNED TEMPERATURE". VSSTAT = "NOT DONE" records are generated for any missed diary days and are flagged with VSDRVFL = "Y".

Non-reactogenicity vital signs have VSCAT = "GENERAL VITAL SIGNS".

A relationship has also been defined between clinical event summary records and temperature vital signs records using CELNKGRP and VSLNKGRP.

QNAM	Description
CLTYP	Collection Type
VSCOLSRT	Collected Summary Result Type

CLTYP in SUPPVS will be "DIARY CARD" for assessments by the subject in the e-diary or "CRF" if recorded by the investigator.

4 Data Conformance Summary

4.1 Conformance Inputs

Was a validator used to evaluate conformance?	**Yes**
If yes, specify the version(s) of the validation rules:	**Pinnacle 21 Enterprise version 4.1.4** **Validation Engine version 1907.2**
Were sponsor-defined validation rules used to evaluate conformance?	**No**
Were the SDTM datasets evaluated in relation to define.xml?	**Yes**
Was define.xml evaluated?	**Yes**

Provide any additional compliance evaluation information:

4.2 Issues Summary

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	AE	736 (47.24%)	New terms were added to extensible codelist EPOCH (C99079) as per the study protocol: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	CE	10424 (19.11%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	CM	114 (63.33%)	New term was added to extensible codelist EPOCH (C99079) for the study protocol needs: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP
CT2002	RACE value not found in 'Race' extensible codelist	Warning	DM	53 (2.34%)	New terms were added to extensible codelist RACE (C74457) as per the study protocol needs: • MULTIPLE
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	DS	3272 (20.55%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • REPEAT SCREENING 1
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	DV	1918 (57.55%)	New terms were added to extensible codelist EPOCH (C99079) as per the study protocol: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	EC	4507 (69.22%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • REPEAT SCREENING 1

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	EX	4507 (69.22%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • REPEAT SCREENING 1
CT2002	EXDOSU value not found in 'Unit' extensible codelist	Warning	EX	6511 (100.00%)	New terms were added to extensible codelist Unit (C71620) as per the study protocol needs: • mcg
CT2002	FAORRESU value not found in 'Unit' extensible codelist	Warning	FA	1390 (0.37%)	New terms were added to extensible codelist Unit (C71620) as per the study protocol needs: • CALIPER UNIT • VISITS/CONTACTS
CT2002	FASTRESU value not found in 'Unit' extensible codelist	Warning	FA	295 (< 0.1%)	New term was added to extensible codelist Unit (C71620) as per the study protocol needs: • VISITS/CONTACTS
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	FA	369458 (98.18%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	HO	3096 (60.48%)	New term was added to extensible codelist EPOCH (C99079) for the study protocol needs: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	IS	1238 (16.11%)	New terms were added to extensible codelist EPOCH (C99079) as per the study protocol: • VACCINATION • REPEAT SCREENING 1
CT2002	ISORRESU value not found in 'Unit' extensible codelist	Warning	IS	7685 (100.00%)	New terms were added to extensible codelist Unit (C71620) as per the study protocol needs: • NA
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	LB	1337 (35.77%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP
CT2002	LBORRESU value not found in 'Unit' extensible codelist	Warning	LB	287 (7.68%)	New terms were added to extensible codelist Unit (C71620) as per the study protocol needs: • 10^3/uL • 10^6/cu mm • /uL
CT2002	MBSPEC value not found in 'Specimen Type' extensible codelist	Warning	MB	19181 (98.30%)	New terms were added to extensible codelist Specimen Type (C78734) for the study protocol needs: • NASAL_SWAB • NASAL_SWAB_SELF • RESPIRATORY SECRETIONS

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	MB	6338 (32.48%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP
CT2002	MBMETHOD value not found in 'Method' extensible codelist	Warning	MB	18148 (93.01%)	New terms were added to extensible codelist METHOD (C85492) as per the study protocol: • NEXT GENERATION SEQUENCING • REVERSE TRANSCRIPTASE PCR
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	MO	2 (66.67%)	New term was added to extensible codelist EPOCH (C99079) for the study protocol needs: • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	SE	4207 (43.22%)	New term was added to extensible codelist EPOCH (C99079) for the study protocol needs: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	SV	12475 (48.33%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • REPEAT SCREENING 1 • OPEN LABEL FOLLOW-UP

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	TA	12 (38.71%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • OPEN LABEL FOLLOW-UP • REPEAT SCREENING 1
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	VS	42888 (99.79%)	New term was added to extensible codelist EPOCH (C99079) as per the study protocol needs: • VACCINATION • REPEAT SCREENING 1
CT2005	DSDECOD value not found in 'Completion/Reason for Non-Completion' extensible codelist when DSCAT == 'DISPOSITION EVENT'	Warning	DS	14 (0.21%)	New term was added to extensible codelist NCOMPLT (C66727) for the study protocol needs: • NO LONGER MEETS ELIGIBILITY CRITERIA
CT2005	TSVAL value not found in 'Trial Phase Response' extensible codelist when TSPARMCD == 'TPHASE'	Warning	TS	1 (100.00%)	New term was added to extensible codelist TPHASE (C66737) for the study protocol needs: • PHASE I/II/III TRIAL
CT2005	TSVAL value not found in 'Trial Blinding Schema Response' extensible codelist when TSPARMCD == 'TBLIND'	Warning	TS	1 (100.00%)	New term was added to extensible codelist TBLIND (C66735) for the study protocol needs: • OBSERVER BLIND
SD0002	NULL value in SPDEVID variable marked as Required	Error	DI	2 (2.27%)	This rule fired for 2 records in DI domain where SPDEVID was null. At the time of data extraction study is still ongoing and complete SPDEVID data was not obtained at the time of the snapshot.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD0005	Duplicate value for LBSEQ variable	Error	LB	614 (81.65%)	This is a false positive by P21 and is part of a known issue for SD0005 -- rule logic is flagging falsely (per P21 support). LBSEQ values are unique for each record within LB domain and within each Unique Subject Identifier (USUBJID), Sponsor Defined ID (LBSPID) variables value.
SD0005	Duplicate value for MBSEQ variable	Error	MB	306 (91.62%)	This is a false positive by P21. It is not an issue with MBSEQ but is an issue with not having a unique record for USUBJID and MBSPID -- rule logic is flagging falsely (per P21 support). MBSEQ values are unique for each record within MB domain and within each Unique Subject Identifier (USUBJID), Sponsor Defined Identifier (MBSPID) variables value.
SD0006	No baseline flag record in LB for subject	Warning	DM	1296 (57.32%)	Per protocol safety lab data is not collected for Phase 2/3. Lab data could be collected for COVID illness visits, which are during study conduct and will not be used to set the baseline flag.
SD0006	No baseline flag record in MB for subject	Warning	DM	1 (< 0.1%)	For this 1 subjects microbiology data is not collected.
SD0007	Inconsistent value for Standard Units	Error	LB	26 (4.02%)	This check fired for several lab tests with inconsistencies in standard units. As a standard course of action, laboratory unit inconsistencies are reviewed by the clinical team. At the time of data extraction, study is still ongoing and the check may not have been completed at the time of this data snapshot.
SD0016	Missing value for FASTRESC, when FADRVFL='Y'	Warning	FA	43600 (97.71%)	As per CBER guidance, the records were derived for missed diary days and FADRVFL flag is used to indicate that data was not collected.
SD0016	Missing value for VSSTRESC, when VSDRVFL='Y'	Warning	VS	4360 (100.00%)	As per CBER guidance, the records were derived for missed diary days and VSDRVFL flag is used to indicate that data was not collected.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD0021	Missing End Time-Point value	Warning	CE	169 (0.31%)	Start and End dates are missing as they are not collected so the reference timepoint values will be missing as well.
SD0021	Missing End Time-Point value	Warning	CM	178 (98.89%)	No End Date/Time captured in CONCOMITANT MEDICATIONS - BASELINE (CONMED BSL) and CONCOMITANT MEDICATIONS - NON STUDY VACCINATIONS (CONMED VAX).
SD0021	Missing End Time-Point value	Warning	HO	295 (5.76%)	For 295 records Start and End dates are missing as they are not collected on the HEALTHCARE UTILIZATION ASSESSMENT CRF
SD0022	Missing Start Time-Point value	Warning	CE	169 (0.31%)	CESTDTC is missing for CECAT='REACTOGENICITY' or 'EFFICACY' where CEOCCUR='N' and is as per the CBER/OVRR flat model implementation. For CECAT = "EFFICACY" where CEOCCUR='N', CESTDTC is not collected on the CRF "Illness Details" page.
SD0022	Missing Start Time-Point value	Warning	HO	295 (5.76%)	For 295 records Start and End dates are missing as they are not collected on the HEALTHCARE UTILIZATION ASSESSMENT CRF
SD0027	Missing value for VSORRES, when VSORRESU is provided	Warning	VS	1 (< 0.1%)	Incorrect information entered at site, the values will remain missing per site confirmation.
SD0030	Missing value for VSSTRESC, when VSSTRESU is provided	Warning	VS	1 (< 0.1%)	Incorrect information entered at site in VSORRES, since VSSTRESC is derived from VSORRES and since VSORRES is missing for this subject, the values will remain missing for this submission.
SD0041	Value for CEOCCUR is populated for unsolicited Intervention or Event	Error	CE	4648 (97.79%)	At the request of CBER, records with CETERM=COVID-19 like illness and COVID-19 have been added for all subjects, with CEOCCUR = Y or N. These are considered derived records rather than spontaneous. (References: IND 19736.92).
SD0057	SDTM Expected variable ISSTRESN not found	Warning	IS	1 (100.00%)	ISORRES has values as "POS" and "NEG", no numerical values present to be mapped into ISSTRESN.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD0057	SDTM Expected variable ISSTRESU not found	Warning	IS	1 (100.00%)	Units for test values were "NA" in the lab file and were not mapped into the IS domain.
SD0065	USUBJID/VISIT/VISITNUM values do not match SV domain data	Warning	CE	2 (0.17%)	For subject 10131872: covid-19 symptoms starting date is not going to show up in SV. He only came for assessment on 8SEP and as it was beyond cutoff date of 2SEP its not going to show up in SV. He has 30AUG in CE, as that was the symptom starting date and not the visit date. For subject 11421346: the data filled late by the site, will remain as is. Explanation as per study team's email: Mon 25-10-2021 15:21
SD0065	USUBJID/VISIT/VISITNUM values do not match SV domain data	Warning	MB	1 (< 0.1%)	For subject 11421346: the data filled late by the site, will remain as is. Explanation as per study team's email: Mon 25-10-2021 15:21
SD0072	Invalid RDOMAIN	Error	RELREC	297 (49.17%)	As per SDTM IG 3.2 section 4.1.1.7 Splitting Domains: "In RELREC, if a dataset level relationship is defined for a split Findings About domain, then RDOMAIN may contain the four-character dataset name". P21 doesn't recognize FACE or FAHO as valid RDOMAINS.
SD0080	AE start date is after the latest Disposition date	Error	AE	34 (2.18%)	At the time of data extraction, study is still ongoing and disposition status is collected at the completion or discontinuation of each stage of the study therefore may not have occurred at the time of this data snapshot.
SD0082	Exposure end date is after the latest Disposition date	Warning	EX	59 (0.91%)	At the time of data extraction, study is still ongoing and disposition status is collected at the completion or discontinuation of each stage of the study therefore may not have occurred at the time of this data snapshot.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1023	VISIT/VISITNUM values do not match TV domain data	Warning	MB	3 (< 0.1%)	These records having VISIT=COVID_AR1, COVID_BR1 are illness visits and considered unplanned and not included in the TV domain.
SD1082	Variable length is too long for actual data	Error	CE	1 (2.94%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	CO	4 (40.00%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	DM	1 (4.00%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	EC	1 (5.00%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1082	Variable length is too long for actual data	Error	EX	1 (5.26%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	FA	1 (3.13%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	HO	1 (5.56%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	IE	2 (16.67%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1082	Variable length is too long for actual data	Error	IS	1 (5.56%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. Pinnacle 21 provides false positive information since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	LB	2 (7.69%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	MB	2 (8.33%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. This is a Pinnacle 21 false positive issue since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	MH	2 (10.53%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. Pinnacle 21 provides false positive information since it only checks the length of the variable within the data set.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1082	Variable length is too long for actual data	Error	MO	1 (6.67%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. Pinnacle 21 provides false positive information since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	SV	1 (12.50%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. Pinnacle 21 provides false positive information since it only checks the length of the variable within the data set.
SD1082	Variable length is too long for actual data	Error	VS	1 (3.33%)	According to FDA technical conformance guide section 3.3.3: The allotted length for each column containing character (text) data should be set to the maximum length of the variable used across all datasets in the study except for suppqual datasets. Pinnacle 21 provides false positive information since it only checks the length of the variable within the data set.
SD1097	No Treatment Emergent info for Adverse Event	Warning	AE	1558 (100.00%)	In Vaccine studies Treatment Emergent flag is not required per communication from CBER/OVRR.
SD1117	Duplicate records	Warning	FA	1 (< 0.1%)	The FAOBJ which appears to be duplicate for records, which are not pre-specified for collection on the CRF, however the verbatim term is unique for these records and are coded to same preferred term.
SD1124	Missing value for FAREASND, when FASTAT is 'NOT DONE'	Warning	FA	11 (< 0.1%)	Reason for NOT DONE for variable FAREASND is not collected on the CRF.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1124	Missing value for LBREASND, when LBSTAT is 'NOT DONE'	Warning	LB	263 (100.00%)	Reason for NOT DONE for variable LBREASND is not collected on the CRF.
SD1124	Missing value for VSREASND, when VSSTAT is 'NOT DONE'	Warning	VS	9 (0.21%)	Reason for NOT DONE for variable VSREASND is not collected on the CRF
SD1143	No Details info for AESMIE Adverse Event in SUPPAE domain	Warning	AE	5 (100.00%)	The CRF is not designed with a free text "other specify" field to capture the description of Other Medically Important Serious Adverse Events. The description details are the AETERM/AEDECOD and therefore AESOSP is not mapped to SUPPAE.
SD1201	Duplicate records in CE domain	Warning	CE	17473 (32.04%)	CETPTREF is different for all specified CETERMs either VACCINATION 1, VACCINATION 2 . Therefore, these records are not true duplicates.
SD1201	Duplicate records in DS domain	Warning	DS	16 (0.10%)	Duplicate dates are expected in DS domain.
SD1201	Duplicate records in DV domain	Warning	DV	322 (9.66%)	DVSPID values are unique for these records. Therefore, these are not true duplicates.
SD1202	AESTDTC date is after RFPENDTC	Error	AE	6 (0.43%)	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.
SD1202	CMSTDTC date is after RFPENDTC	Error	CM	4 (2.50%)	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.
SD1202	DVSTDTC date is after RFPENDTC	Error	DV	16 (0.53%)	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.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1203	CODTC date is after RFPENDTC	Error	CO	1 (< 0.1%)	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.
SD1203	ISDTC date is after RFPENDTC	Error	IS	1 (< 0.1%)	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.
SD1203	LBDTC date is after RFPENDTC	Error	LB	17 (0.54%)	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.
SD1203	MBDTC date is after RFPENDTC	Error	MB	54 (0.31%)	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.
SD1204	AEENDTC date is after RFPENDTC	Error	AE	3 (0.23%)	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.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1204	CEENDTC date is after RFPENDTC	Error	CE	105 (1.07%)	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.
SD1204	CMENDTC date is after RFPENDTC	Error	CM	1 (100.00%)	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.
SD1234	Missing TYPE Parameter for Device	Error	DI	44 (100.00%)	Device Type Parameter information is not available for the Medical Device used in the study.
SD1258	RFSTDTC is populated for subject who did not receive treatment	Warning	DM	4 (100.00%)	There were subjects that were randomized but not treated. Therefore, RFSTDTC was populated for those records when ACTARM was 'Not Treated'. the actual dosing start date RFXSTDTC is not populated
SD1274	HOTERM equals 'OTHER'	Warning	HO	812 (15.86%)	OTHER is a collected term used in the HEALTH CARE UTILIZATION crf form.
SD1282	ECTPTREF variable is present when ECELTM, ECTPTNUM, and ECTPT are missing	Error	EC	1 (100.00%)	Based on CDISC TAUG, ECTPTREF can be populated for Vaccine studies; ECELTM, ECTPTNUM, and ECTPT are not necessary.
SD1282	EXTPTREF variable is present when EXELTM, EXTPTNUM, and EXTPT are missing	Error	EX	1 (100.00%)	Based on CDISC TAUG, EXTPTREF can be populated for Vaccine studies; EXELTM, EXTPTNUM, and EXTPT are not necessary.
SD1299	No timing variables are present in dataset	Warning	DI	1 (100.00%)	In the SDTMIG-3.2 the DI domain does not list any timing variables, moreover since Device Identifiers are study level data rather than subject level data, timing variables are not expected.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1319	DVSTDTC is before RFICDTC	Error	DV	11 (0.33%)	These 11 records are flagged due to various protocol deviations occurred before the Informed Consent was signed or Consent date was collected/entered into the system. Data is being reported as collected.
SD1331	DSSTDTC is after DSDTC	Error	DS	3 (< 0.1%)	Data is reported as collected. This rule fired 3 subject ID's, because of temporary delay in vaccination: • C4591001 1009 10091301 • C4591001 1147 11471261 • C4591001 1147 11471262
SD1339	Missing EPOCH value, when a start or observation date is provided	Warning	CE	385 (3.45%)	For events domains --STDTC is used to derive EPOCH. Since CESTDTC is missing for these records, EPOCH is not derived.
SD1339	Missing EPOCH value, when a start or observation date is provided	Warning	HO	1 (< 0.1%)	For HO domain --DTC is used to derive EPOCH. Since HODTC is missing for these records, EPOCH is not derived.
SD1354	ARMCD value not present in DM	Error	TA	22 (70.97%)	Current TA ARMCD has the randomized codes based on the protocol, including the 12 - 15 age group randomization codes in Phase 2/3. Only the randomization code for subject in 12 - 15 age group - phase 2/3 are included in DM.ARMCD while the rest (B1_10, B1_100, B1_20, B1_30, B2_10, B2_20, B2_30) are not applicable in this submission.
SD1375	RFENDTC is populated for subject who did not receive treatment	Warning	DM	4 (100.00%)	There were subjects that were randomized but not treated. Therefore, RFENDTC was populated for those records when ACTARM was 'Not Treated'. the actual dosing end date RFXENDTC is not populated

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1379	ETCD value not present in SE	Error	TE	6 (50.00%)	Current TE ETCD has all the trial elements based on the protocol. The trial elements below are not in scope for Booster submission. • VAXB1_10 • VAXB1_20 • VAXB1_30 • VAXB1100 • VAXB2_10 • VAXB2_20
SD2236	ACTARMCD does not equal ARMCD	Warning	DM	4 (0.18%)	There were subjects that were randomized but not treated. Therefore, ARMCD (planned) has a different value than ACTARMCD (actual), since these were not treated the ACTARMCD has values = "NOTTRT".
SD2237	ACTARM does not equal ARM	Warning	DM	4 (0.18%)	There were subjects that were randomized but not treated. Therefore, ARM (planned) has a different value than ACTARM (actual), since these were not treated the ACTARM has values = "Not Treated".
SD2239	Inconsistent value for FATPT	Error	FA	611 (0.16%)	Values are populated correctly as per Vaccine TAUG. P21 rule is expecting same TPT/TPTNUM used across subject/DTC. Since DTC differs, P21 check fired, however there is an inherent assumption in the rule that for different times on same date, the timepoint should be different (e.g. 1 HR and 3 HRS timepoints cannot have same date/time values), which does not apply here.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD2239	Inconsistent value for VSTPT	Error	VS	717 (1.67%)	Values are populated correctly as per Vaccine TAUG. P21 rule is expecting same TPT/TPTNUM used across subject/DTC. Since DTC differs, P21 check fired, however there is an inherent assumption in the rule that for different times on same date, the timepoint should be different (e.g. 1 HR and 3 HRS timepoints cannot have same date/time values), which does not apply here.
SD2243	Invalid TSVCDREF value for PCLAS	Error	TS	1 (100.00%)	Due to the novel nature of the treatment, PCLAS is not available in NDF-RT. TSVAL is set to "Vaccines, Nucleic Acid" from CSP dictionary, CUI number "C0600412" is used in TSVALCD, and "CSP" is used in TSVCDREF.
SD2260	Invalid TSVAL value for TRT	Error	TS	2 (100.00%)	Due to the novel nature of the treatment, there is no standard name for BNT162b1/BNT162b2 from FDA substance registration system.
SD2261	Invalid TSVALCD value for TRT	Error	TS	2 (100.00%)	There is no corresponding code for BNT162b1/BNT162b2 from UNII
SD2263	Invalid TSVAL value for PCLAS	Error	TS	1 (100.00%)	Due to the novel nature of the treatment, NDF-RT TSVAL is set to "Vaccines, Nucleic Acid" from CSP dictionary. And CUI number "C0600412" is used in TSVALCD.
SD2264	Invalid TSVALCD value for PCLAS	Error	TS	1 (100.00%)	Due to the novel nature of the treatment, PCLAS is not available in NDF-RT. TSVAL is set to "Vaccines, Nucleic Acid" from CSP dictionary. And CUI number "C0600412" is used in TSVALCD.
SD2265	TSVAL/TSVALCD value mismatch for PCLAS	Error	TS	1 (100.00%)	Due to the novel nature of the treatment, TSPARMCD=PCLAS is not available in NDF-RT. TSVAL is set to "Vaccines, Nucleic Acid" from CSP dictionary. And CUI number "C0600412" is used in TSVALCD.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
TS0006	No Baseline (ALT) test results for Subject	Error	DM	2261 (100.00%)	Per protocol safety lab data is not collected for Phase 2/3. Lab data could be collected for COVID illness visits, which would be during study conduct and will not be used to set the baseline flag.
TS0007	No Baseline (ALP) test results for Subject	Error	DM	2261 (100.00%)	Per protocol safety lab data is not collected for Phase 2/3. Lab data could be collected for COVID illness visits, which would be during study conduct and will not be used to set the baseline flag.
TS0008	No Baseline (AST) test results for Subject	Error	DM	2261 (100.00%)	Per protocol safety lab data is not collected for Phase 2/3. Lab data could be collected for COVID illness visits, which would be during study conduct and will not be used to set the baseline flag.
TS0009	No Baseline (BILI) test results for Subject	Error	DM	2261 (100.00%)	Per protocol safety lab data is not collected for Phase 2/3. Lab data could be collected for COVID illness visits, which would be during study conduct and will not be used to set the baseline flag.
TS0012	Analysis Required variable AESEV not found	Error	AE	1 (100.00%)	AESEV not collected in the CRF for the study. AETOXGR (Toxicity Grade) variable used for severity.
TS0039	No (ALT) test results	Error	DM	2230 (98.63%)	Per protocol (ALT test results) are not collected for Phase 2/3. Though it could be collected for COVID illness visits.
TS0040	No (ALP) test results	Error	DM	2230 (98.63%)	Per protocol (ALP test results) are not collected for Phase 2/3. Though it could be collected for COVID illness visits.
TS0041	No (AST) test results	Error	DM	2230 (98.63%)	Per protocol (AST test results) are not collected for Phase 2/3. Though it could be collected for COVID illness visits.
TS0042	No (BILI) test results	Error	DM	2230 (98.63%)	Per protocol (BILI test results) are not collected for Phase 2/3. Though it could be collected for COVID illness visits.
TS0047	No (SYSBP) test results for subject	Error	DM	2241 (99.12%)	Per protocol blood pressure is not collected for Phase 2/3, though it could be collected for COVID illness visits.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
TS0048	No (DIABP) test results for subject	Error	DM	2241 (99.12%)	Per protocol blood pressure is not collected for Phase 2/3, though it could be collected for COVID illness visits.
TS0049	No (HR) or (PULSE) test results for subject	Error	DM	2241 (99.12%)	Per protocol HR/PULSE test results are not collected for Phase 2/3, though it could be collected for COVID illness visits.
TS0050	Missing PC dataset	Warning	GLOBAL	1 (100.00%)	Not applicable for this submission.
TS0051	Missing PP dataset	Warning	GLOBAL	1 (100.00%)	Not applicable for this submission.
TS0053	Neither AESEV or AETOXGR is populated	Error	AE	480 (30.81%)	Reactogenicity events that are present after the diary period were added to AE domain and severity or toxicity grades were not captured after end of diary period.
TS0057	LBSTRESN is populated but LBSTNRHI is not populated	Warning	LB	1 (0.16%)	Based on site confirmation, some reference ranges were not available and will be missing in this submission.
DD0050	Domain/SASDatasetName mismatch for split dataset	Error	DEFINE	1 (100.00%)	Per SDTM IG v3.2, sponsors may choose to split a domain of topically related information into physically separate datasets. Currently our internal approach is to split FA by topic hence we have dataset with names FACE, SUPPFACE, FAHO.

4.3 Additional Conformance Details

There are no additional details to be documented.

Appendix I: Inclusion/Exclusion Criteria

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion
1.0, 2.0, 5.0	INCLUSION	IN01A00	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study stage)
6.0	INCLUSION	IN01A05	Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study phase)
7.0	INCLUSION	IN01A06	Male or female participants between the ages of 18 and 55 years, inclusive, and 65 and 85 years, inclusive (Phase 1), or >= 16 years (Phase 2/3), at randomization
8.0	INCLUSION	IN01A07	Male or female participants between the ages of 18 and 55 years, inclusive, and 65 and 85 years, inclusive (Phase 1), or >=12 years (Phase 2/3), at randomization. Note that participants <18 years of age cannot be enrolled in the EU
1.0, 2.0, 5.0, 6.0, 7.0, 8.0	INCLUSION	IN02A00	Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures
1.0, 2.0, 5.0	INCLUSION	IN03A00	Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study. Note: Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, can be included

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion
6.0	INCLUSION	IN03A05	Healthy participants who are determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study. Note: Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, can be included
7.0, 8.0	INCLUSION	IN03A06	Healthy participants who are determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study. Note: Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, can be included. Specific criteria for Phase 3 participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV) can be found in Section 10.8
1.0, 2.0, 5.0, 6.0, 7.0	INCLUSION	IN04A00	Capable of giving personal signed informed consent as described in Appendix 1, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol
8.0	INCLUSION	IN04A07	Capable of giving personal signed informed consent/have parent(s)/legal guardian capable of giving signed informed consent as described in Appendix 1, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol
6.0	INCLUSION	IN05A05	Participants who, in the judgment of the investigator, are at risk for acquiring COVID-19
7.0, 8.0	INCLUSION	IN05A06	Phase 2/3 only: Participants who, in the judgment of the investigator, are at higher risk for acquiring COVID-19 (including, but not limited to, use of mass transportation, relevant demographics, front line essential workers and others)

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion
1.0, 2.0, 5.0, 6.0, 7.0, 8.0	EXCLUSION	EX01A00	Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study
1.0, 2.0, 5.0, 6.0	EXCLUSION	EX02A00	Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)
7.0, 8.0	EXCLUSION	EX02A06	Phase 1 & 2 only: Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV)
1.0, 2.0, 5.0, 6.0, 7.0, 8.0	EXCLUSION	EX03A00	History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s)
1.0, 2.0, 5.0, 6.0, 7.0, 8.0	EXCLUSION	EX04A00	Receipt of medications intended to prevent COVID 19
1.0, 2.0, 5.0	EXCLUSION	EX05A00	Stages 1 and 2 only: Previous clinical or microbiological diagnosis of COVID-19
6.0, 7.0	EXCLUSION	EX05A05	Previous clinical or microbiological diagnosis of COVID-19
8.0	EXCLUSION	EX05A07	Previous clinical (based on COVID-19 symptoms/signs alone, if a SARS-CoV-2 NAAT result was not available) or microbiological (based on COVID-19 symptoms/signs and a positive SARS-CoV-2 NAAT result) diagnosis of COVID-19
1.0	EXCLUSION	EX06A00	Sentinel participants in Stage 1 only: Individuals at high risk for severe COVID-19, including those with any of the following risk factors: Hypertension, Diabetes mellitus, Chronic pulmonary disease, Asthma, Current vaping or smoking, History of chronic smoking within the prior year, BMI >30 kg/m2, Anticipating the need for immunosuppressive treatment within the next 6 months

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion
2.0, 5.0	EXCLUSION	EX06A01	Sentinel participants in Stage 1 only: Individuals at high risk for severe COVID-19, including those with any of the following risk factors: Hypertension, Diabetes mellitus, Chronic pulmonary disease, Asthma, Current vaping or smoking, History of chronic smoking within the prior year, Chronic liver disease, Stage 3 or worse chronic kidney disease (glomerular filtration rate <60 mL/min/1.73 m2), Resident in a long-term facility, BMI >30 kg/m2, Anticipating the need for immunosuppressive treatment within the next 6 months
6.0, 7.0, 8.0	EXCLUSION	EX06A05	Phase 1 only: Individuals at high risk for severe COVID-19,including those with any of the following risk factors: Hypertension, Diabetes mellitus, Chronic pulmonary disease, Asthma, Current vaping or smoking, History of chronic smoking within the prior year, Chronic liver disease, Stage 3 or worse chronic kidney disease (glomerular filtration rate <60 mL/min/1.73 m2), Resident in a long-term facility, BMI >30 kg/m2, Anticipating the need for immunosuppressive treatment within the next 6 months
1.0, 2.0, 5.0	EXCLUSION	EX07A00	Sentinel participants in Stage 1 only: Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (eg, healthcare worker, emergency response personnel)
6.0, 7.0, 8.0	EXCLUSION	EX07A05	Phase 1 only: Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (eg, healthcare worker, emergency response personnel)
1.0, 2.0, 5.0, 6.0, 7.0, 8.0	EXCLUSION	EX08A00	Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.
1.0, 2.0	EXCLUSION	EX09A00	Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention including but not limited to: systemic or cutaneous lupus erythematosus, autoimmune arthritis/rheumatoid arthritis, Guillain-Barre syndrome, multiple sclerosis, Sjogren's syndrome, idiopathic thrombocytopenia purpura, glomerulonephritis, autoimmune thyroiditis, giant cell arteritis (temporal arteritis), psoriasis, and insulin-dependent diabetes mellitus (type 1)

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion
5.0	EXCLUSION	EX09A04	Sentinel participants in Stage 1 only: Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention, including but not limited to: systemic or cutaneous lupus erythematosus, autoimmune arthritis/rheumatoid arthritis, Guillain-Barre syndrome, multiple sclerosis, Sjogren's syndrome, idiopathic thrombocytopenia purpura, glomerulonephritis, autoimmune thyroiditis, giant cell arteritis (temporal arteritis), psoriasis, and insulin-dependent diabetes mellitus (type 1)
6.0, 7.0, 8.0	EXCLUSION	EX09A05	Phase 1 only: Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention, including but not limited to: systemic or cutaneous lupus erythematosus, autoimmune arthritis/rheumatoid arthritis, Guillain-Barre syndrome, multiple sclerosis, Sjogren's syndrome, idiopathic thrombocytopenia purpura, glomerulonephritis, autoimmune thyroiditis, giant cell arteritis (temporal arteritis), psoriasis, and insulin-dependent diabetes mellitus (type 1)
1.0, 2.0, 5.0, 6.0, 7.0, 8.0	EXCLUSION	EX10A00	Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection
1.0, 2.0, 5.0, 6.0, 7.0, 8.0	EXCLUSION	EX11A00	Women who are pregnant or breastfeeding
1.0, 2.0, 5.0, 6.0, 7.0, 8.0	EXCLUSION	EX12A00	Previous vaccination with any coronavirus vaccine

1.0	EXCLUSION	EX13A00	Individuals who receive treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, eg, for cancer or an autoimmune disease, or planned receipt throughout the study. If systemic corticosteroids have been administered short term (<14 days) for treatment of an acute illness, participants should not be enrolled into the study until corticosteroid therapy has been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids are permitted

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion
2.0	EXCLUSION	EX13A01	Individuals who receive treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, eg, for cancer or an autoimmune disease, or planned receipt throughout the study. If systemic corticosteroids have been administered short term (<14 days) for treatment of an acute illness, participants should not be enrolled into the study until corticosteroid therapy has been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized (except for sentinel subjects in Stage 1 – see exclusion 14), intra-articular, intrabursal, or topical (skin or eyes) corticosteroids are permitted
1.0	EXCLUSION	EX14A00	Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study
1.0	EXCLUSION	EX15A00	Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation
1.0	EXCLUSION	EX16A00	Previous participation in other studies involving study intervention containing lipid nanoparticles
1.0	EXCLUSION	EX17A00	Sentinel participants in Stage 1 only: Positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the screening visit
6.0	EXCLUSION	EX17A05	Phase 1 only: Positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the screening visit
1.0	EXCLUSION	EX18A00	Sentinel participants in Stage 1 only: Any screening hematology and/or blood chemistry laboratory value that meets the definition of a >=Grade 1 abnormality. Note: With the exception of bilirubin, participants with any stable Grade 1 abnormalities (according to the toxicity grading scale) may be considered eligible at the discretion of the investigator. (Note: A "stable" Grade 1 laboratory abnormality is defined as a report of Grade 1 on an initial blood sample that remains <=Grade 1 upon repeat testing on a second sample from the same participant)

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion
6.0	EXCLUSION	EX18A05	Phase 1 only: Any screening hematology and/or blood chemistry laboratory value that meets the definition of a >= Grade 1 abnormality Note: With the exception of bilirubin, participants with any stable Grade 1 abnormalities (according to the toxicity grading scale) may be considered eligible at the discretion of the investigator. (Note: A "stable" Grade 1 laboratory abnormality is defined as a report of Grade 1 on an initial blood sample that remains <= Grade 1 upon repeat testing on a second sample from the same participant.)
1.0	EXCLUSION	EX19A00	Sentinel participants in Stage 1 only: Positive test for HIV, hepatitis B surface antigen (HBsAg), hepatitis B core antibodies (HBc Abs), or hepatitis C virus antibodies (HCV Abs) at the screening visit
6.0	EXCLUSION	EX19A05	Phase 1 only: Positive test for HIV, hepatitis B surface antigen (HBsAg), hepatitis B core antibodies (HBc Abs), or hepatitis C virus antibodies (HCV Abs) at the screening visit
1.0	EXCLUSION	EX20A00	Sentinel participants in Stage 1 only: SARS-CoV-2 NAAT-positive nasal swab within 24 hours before receipt of study intervention
6.0	EXCLUSION	EX20A05	Phase 1 only: SARS-CoV-2 NAAT-positive nasal swab within 24 hours before receipt of study intervention
1.0	EXCLUSION	EX21A00	Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members
7.0	EXCLUSION	EX21A06	Investigator site staff or Pfizer/BioNTech employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members
2.0	EXCLUSION	EX22A01	Sentinel participants in Stage 1 only: Regular receipt of inhaled/nebulized corticosteroids.

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion
6.0	EXCLUSION	EX22A05	Phase 1 only: Regular receipt of inhaled/nebulized corticosteroids

Appendix II: Data Cutoff Algorithm in Standard Domains

Records are included in SDTM datasets as specified below with &cutoff equal to 02 September 2021

SDTM Domain	Cutoff Description

AE	Apply util_partial_datetime_imputation.sas to AESTDTC and AEENDTC to derive ASTDT AND AENDT respectively.
	%util_partial_datetime_imputation(
	_isodate =AESTDTC/AEENDTC
	,_impdate = ASTDT/AENDT
	,_impdateflag = %str(ASTDTF/AENDTF)
	,_imputation_rule_date = %str(START/STOP));
	
	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'
	- AESDTH = 'N'
	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

SDTM Domain	Cutoff Description

DM	Include all records with DMDTC <= &cutoff
	
	If RFPENDTC > &cutoff then RFPENDTC = ' '
	If RFSTDTC > &cutoff then do;
	If randomization date > &cutoff then do;
	RFSTDTC=' '; RFENDTC=' '; RFXSTDTC=' '; RFXENDTC=' ';
	arm='NOT ASSIGNED'; armcd='NOTASSGN';
	end;
	else if randomization date <= &cutoff then do;
	set RFSTDTC = randomization date;
	RFENDTC=randomization date; RFXSTDTC='';
	RFXENDTC=' ';
	end;
	Else if RFSTDTC <= &cutoff then do;
	If RFENDTC > &cutoff then set RFENDTC=&cutoff;
	RFXENDTC=&cutoff;
	
	If DTHDTC > &cutoff then do;
	set DTHDTC = ' ';
	set DTHFL = ' ';
	end;

EC	Include all records with ECSTDTC <= &cutoff If ECENDTC > &cutoff then do; ECENDTC = &cutoff; ECENDY = ECENDTC – RFSTDTC +1; end;
EX	Include all records with EXSTDTC <= &cutoff If EXENDTC > &cutoff then do; EXENDTC = &cutoff; EXENDY = EXENDTC – RFSTDTC +1; end;
CE/DV/FACE/FAHO/HO/IE/IS/LB/MB/MO/SV/VS/SE	Include all records with (CEDTC/ DVSTDTC/ (Datepart) FADTC /HODTC/ IEDTC/ ISDTC/ (datepart) LBDTC/ MBDTC/ MODTC/ SVSTDTC/ VSDTC/ SESTDTC) <= &cutoff

SDTM Domain	Cutoff Description
DS/MH	Include all records with DSDTC <= &cutoff and (DSSTDTC/ MHSTDTC) <= &cutoff

CM	Apply util_partial_datetime_imputation.sas to CMSTDTC and CMENDTC to derive ASTDT AND AENDT respectively.
	%util_partial_datetime_imputation(
	_isodate =CMSTDTC/CMENDTC
	,_impdate = ASTDT/AENDT
	,_impdateflag = %str(ASTDTF/AENDTF)
	,_imputation_rule_date = %str(START/STOP));
	
	All records with ASTDT <= &cutoff are included.
	In addition,
	
	If .<ASTDT <= &cutoff and AENDT > cutoff date, then
	- CMENDTC is set to missing
	- CMENRTPT = 'ONGOING'
	- CMENTPT = 'Last Subject Encounter'
	-
	end;
	else if CMSTDTC = ' ' and CMENDTC ne ' ' and CMENDTC<= &cutoff then the record is included.
	If CMSTDTC and CMENDTC are both missing then the record is included.
	DROP ASTDT and AENDT

CO	If RDOMAIN = 'IS' then retain all obs where CODTC<= cutoff, else for all other values of RDOMAIN, match with USUBJID /SEQ.

SDTM Domain	Cutoff Description
RELREC	Include all records If USUBJID = ' '. for each domain in RDOMAIN, match with USUBJID /SEQ if index(idvar,'SEQ')>0; else match with USUBJID/LNKID if index(idvar,'LNKID')>0.