Analysis Data Reviewer's Guide

ModernaTX, Inc.

Study mRNA-1273-P301

Analysis Data Reviewer's Guide

Contents

1. Introduction

1.1 Purpose

This document provides context for the analysis datasets and terminology that benefit from additional explanation beyond the Data Definition document (define.xml) for study mRNA-1273-P301. In addition, this document provides a summary of ADaM conformance findings, conversion to SDTM and then to ADaM.

1.2 Acronyms

Acronym	Translation
AR	Adverse Reaction
EDCD	Efficacy Date cutoff date
mRNA	Messenger ribonucleic acid
mITT	Modified Intent-to-Treat

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	•SDTM v1.4 •SDTM-IG v3.2
SDTM Controlled Terminology	CDISC SDTM Controlled Terminology, 2020-09-25
ADaM	•ADaM v2.1 •ADaM-IG v1.1
ADaM Controlled Terminology	CDISC ADaM Controlled Terminology, 2020-09-25
Data Definitions	Define-XML v2.0
TAUG (if applicable)	TAUG-VX 1.1
Medical Events Dictionary	MedDRA 23.0
Other standards (optional)	Guidance for Industry - Technical Specifications Document: Submitting Study Datasets for Vaccines to the Office of Vaccines Research and Review (October 2019)

2. Protocol Description

2.1 Protocol Number and Title

Protocol Number: mRNA-1273-P301

Protocol Title: A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older

Protocol Versions: Amendments 1-8

Amendment 1, 26 Jun 2020
The main purpose of this amendment is to provide more intensive surveillance of symptoms and severity of cases of COVID-19 after the first dose of investigational product.

Amendment 2, 31 Jul 2020
The main purpose of this amendment is to provide more intensive surveillance of symptoms and severity of cases of COVID-19 after the first dose of investigational product.

Amendment 3, 20 Aug 2020
The main purpose of this amendment is to make changes to the protocol in response to feedback from CBER.

Amendment 4, 30 Sep 2020
The main purpose of this amendment is to increase the upper limit for stratification of enrolled participants considered "at risk" at Screening to 50%.

Amendment 5, 11 Nov 2020
The main purpose of this amendment is to clarify that the eDiary prompts for safety surveillance will be weekly and to add Month 19 safety call.

Amendment 6, 23 Dec 2020
The purpose of this amendment is to inform all ongoing study participants of the availability of and eligibility criteria of any COVID-19 vaccine made available under an Emergency Use Authorization (EUA) and to offer participants who originally received placebo in this study the potential benefit of vaccination against COVID-19, given that the primary efficacy endpoint for mRNA-1273 against COVID-19 was met per the protocol-defined interim analysis.

Amendment 7, 10 Feb 2021
The purpose of this amendment is to collect safety information on suspected cases of anaphylaxis and to include participant history of facial injections or dermal fillers in the eDiary.

Amendment 8, 23 Mar 2021
The purpose of this amendment is to update language around unblinding and open-label dosing in the context of the majority of participants already having completed their blinded follow-up. In addition, the amendment updates the reporting of serious COVID-19 cases.

2.2 Protocol Design in Relation to ADaM Concepts

Figure 1: Study Flow Diagram: Part A, the Blinded Phase followed by Part B, the Open-Label Observational Phase

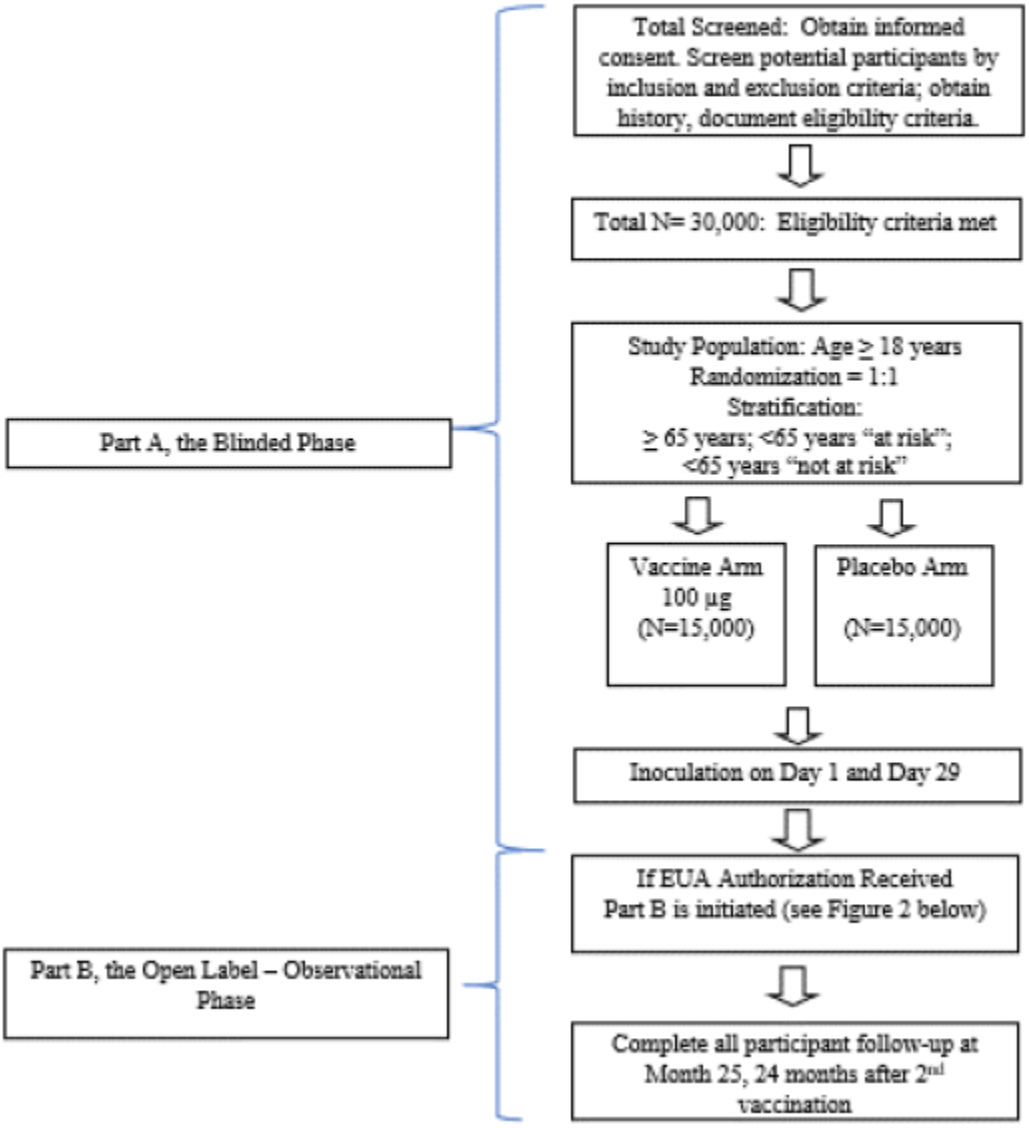
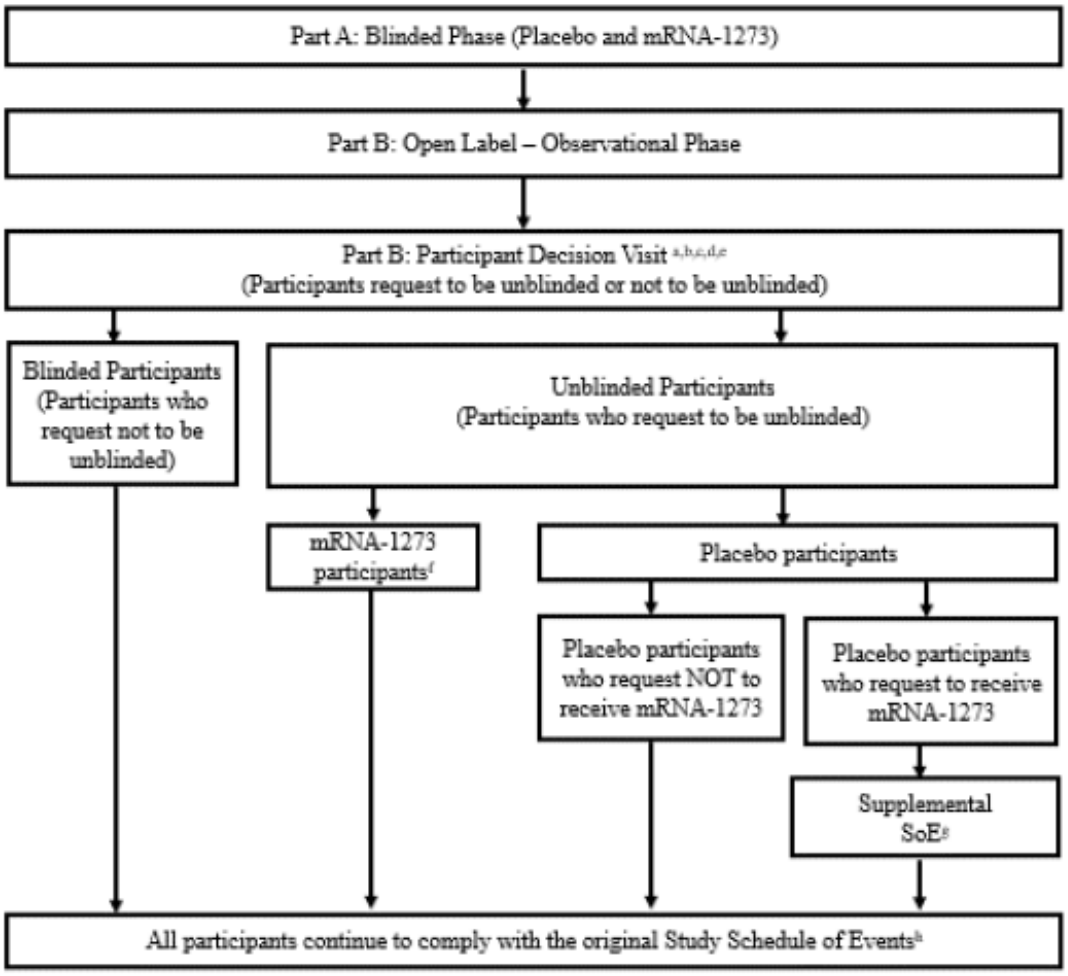


Figure 2: Part B, the Open-Label Observational Phase



[a] All participants are encouraged to remain in the study.
[b] All participants are given the option to be unblinded to treatment received in Part A: Blinded Phase.
[c] All participants are counselled about the importance of continuing other public health measures to limit the spread of disease including physical-social distancing, wearing a mask, and hand-washing.
[d] All participants sign a revised ICF.
[e] All participants consent to provide a nasopharyngeal swab and a blood sample for immunologic analysis.
[f] mRNA-1273 recipients who only received one dose of the mRNA-1273 vaccine will receive the second dose of mRNA-1273 vaccine. Additional details provided in the Supplemental Schedule of Events
[g] Placebo recipients who request to receive mRNA-1273 and meet eligibility, will comply with a Supplemental Schedule of Events in addition to the Original Study Schedule of Events.
[h] Original Study Schedule of Events

3. Analysis Considerations Related to Multiple Analysis Datasets

3.1 Core Variables

Core variables are those that are represented across all/most analysis datasets.

Variable Name	Variable Description
STUDYID	Study Identifier
USUBJID	Unique Subject Identifier
SUBJID	Subject Identifier for the Study
SITEID	Study Site Identifier
COUNTRY	Country
AGE	Age
AGEU	Age Units
STRATAR	Strata Used for Randomization
STRATARN	Strata Used for Randomization (N)
AGEGR1	Pooled Age Group 1
AGEGR1N	Pooled Age Group 1 (N)
AGEGR2	Pooled Age Group 2
AGEGR2N	Pooled Age Group 2 (N)
AGEGR3	Pooled Age Group 3
AGEGR3N	Pooled Age Group 3 (N)
AGEGR4	Pooled Age Group 4
AGEGR4N	Pooled Age Group 4 (N)
SEX	Sex
RACE	Race
RACESPY	Race Specify
ETHNIC	Ethnicity
RANDFL	Randomized Population Flag
FASFL	Full Analysis Set Population Flag
SAFFL	Safety Population Flag

Variable Name	Variable Description
SAR1FL	First Solicited Safety Population Flag
SAR2FL	Second Solicited Safety Population Flag
SARAFL	Solicited Safety Population Flag
MITTFL	Modified Intent to Treat Population Flag
PPROTFL	Per-Protocol Population Flag
RANDIGFL	Random Immunogenicity Subcohort Flag
PPSIFL	Per-Protocol Random Subcohort for IG
CCIASFL	Case-Cohort IG Analysis Set Flag
DOSE1FL	Vaccination 1 Flag
DOSE2FL	Vaccination 2 Flag
OLDOS1FL	OL Vaccination 1 Flag
OLDOS2FL	OL Vaccination 2 Flag
RTPCRBL	Baseline RT-PCR Test
ELECSBL	Baseline Elecsys SARS Cov-2 Assay
SCOV2BL	Baseline SARS-CoV-2 Status
TRT01P	Planned Treatment for Period 01
TRT01PN	Planned Treatment for Period 01 (N)
TRT01A	Actual Treatment for Period 01
TRT01AN	Actual Treatment for Period 01 (N)
TRT02P	Planned Treatment for Period 02
TRT02PN	Planned Treatment for Period 02 (N)
TRT02A	Actual Treatment for Period 02
TRT02AN	Actual Treatment for Period 02 (N)
TR01SDT	Date of First Exposure in Period 01
TR01SDTM	Datetime of First Exposure in Period 01
TRTSEQP	Planned Sequence of Treatments
TRTSEQPN	Planned Sequence of Treatments (N)
TRTSEQA	Actual Sequence of Treatments
TRTSEQAN	Actual Sequence of Treatments (N)

Variable Name	Variable Description
TRTSDT	Date of First Exposure to Treatment
TRTEDT	Date of Last Exposure to Treatment
TR01EDT	Date of Last Exposure in Period 01
TR01EDTM	Datetime of Last Exposure in Period 01
DOSE2DT	Date of Dose 2 in Blinded Phase
DOS2DTM	Datetime of Dose 2 in Blinded Phase
TR02SDT	Date of First Exposure in Period 02
TR02SDTM	Datetime of First Exposure in Period 02
TR02EDT	Date of Last Exposure in Period 02
TR02EDTM	Datetime of Last Exposure in Period 02
OLDOS2DT	Date of Dose 2 in Open Label Phase
OLDO2DTM	Datetime of Dose 2 in Open Label Phase
EUAVACDT	Date of Post-EUA Off-Study COVID Vaccine
EFFCODT	Efficacy Date Cutoff Date
AP01SDT	Period 01 Start Date
AP01EDT	Period 01 End Date
AP02SDT	Period 02 Start Date
AP02EDT	Period 02 End Date
AP01SSDT	Period 01 Start Date for Safety Analysis
AP01SEDT	Period 01 End Date for Safety Analysis
AP02SSDT	Period 02 Start Date for Safety Analysis
AP02SEDT	Period 02 End Date for Safety Analysis
RSKF1	Risk Factor 1
RSKF2	Risk Factor 2
RSKF3	Risk Factor 3
RSKF4	Risk Factor 4
RSKF5	Risk Factor 5
RSKF6	Risk Factor 6
STRATAV	Strata from Verification Source

Variable Name	Variable Description
STRATAVN	Strata from Verification Source (N)
STUDDUR3	Study Duration 3
MINORITY	Minority
RACEGR1	Pooled Race Group 1
RACEGR1N	Pooled Race Group 1 (N)
RISKGR1	Pooled Risk Group 1
RISKGR1N	Pooled Risk Group 1 (N)
RETHGR1	Pooled Race and Ethnicity Group 1
RETHGR1N	Pooled Race and Ethnicity Group 1 (N)
CVDSVAFL	Severe COVID-19 Based on Adj Flag
COVIDAFL	COVID-19 Based on Adjudication Flag

3.2 Treatment Variables

ARM versus TRT01P

Are the values of ARM equivalent in meaning to values of TRT01P?

No, ARM is based on planed treatment in both blinded phase and open label phase, but TRT01P is defined as planned treatment that is based on randomization number in blinded phase only

ACTARM versus TRT01A

If TRT01A is used, then are the values of ACTARM equivalent in meaning to values of TRT01A?

No, ACTARM is based on actual treatment in both blinded phase and open label phase, but TRT01A is actual treatment is based on subject received actual treatment in blinded phase only

Use of ADaM Treatment Variables in Analysis

Are both planned and actual treatment variables used in analysis?

Yes, Treatment Variables are used by each analysis

Treatment	Population Set
TRT01P	Randomization Set
TRT01P	Full Analysis Set
TRT01A/TRTSEQA	Safety Set
TRT01A	Solicited Safety Set
TRT01P/TRTSEQP	Modified Intent-to-Treat Set
TRT01P/TRTSEQP	Per-Protocol Set

Use of ADaM Treatment Grouping Variables in Analysis

Are both planned and actual treatment grouping variables used in analysis?

No, there are no treatment grouping variables created in analysis

3.3 Subject Issues that Require Special Analysis Rules

1. Duplicated Enrollment Issues

First Instance: The same subject was randomized twice

- Subject US3902081 is the same subject as US3902125. The same subject is not allowed to be randomized twice. Only the first randomization and first assigned subject number US3902081 should be used for this subject. The second randomization and subject number US3902125 will be considered invalid.
- Protocol deviation for US3902125 due to the wrong randomization will be classified as "Significant" and "Exclude from all analyses sets". Biostatistics/Programming will exclude US3902125 from all analyses.

Second Instance: Wrong randomization

- Subject US3522029 is the same subject as US3522027. Only subject number US3522029 should be used for this subject, subject number US3522027 will be considered invalid. The unblinded team confirmed that the treatment assignments from both subject numbers per IRT were the same coincidently. As a result, this subject was dosed with the same treatment.
- Protocol deviation for US3522027 due to the wrong randomization will be classified as "Significant" and "Exclude from all analyses sets". Biostatistics/Programming will exclude US3522027 from all analyses.

Third Instance: The same subject was enrolled at two sites

- Protocol deviation for US3172082 due to being enrolled/dosed at two sites will be classified as "Significant".
- Protocol deviation for US3352166 due to being enrolled/dosed at two sites will be classified as "Significant" and "Exclude from all analyses sets". Biostatistics/Programming will exclude US3352166 from all analyses.

Fourth Instance: The same subject was enrolled at two sites

- Protocol deviation for US3352442 due to being enrolled/dosed at two sites will be classified as "Significant".
- Protocol deviation for US3172220 due to being enrolled/dosed at two sites will be classified as "Significant" and "Exclude from all analyses sets". Biostatistics/Programming will exclude US3172220 from all analyses.

Fifth Instance: The same subject was enrolled at two sites

- Protocol deviation for US3732072 due to being enrolled/dosed at two sites will be classified as "Significant".
- Protocol deviation for US3162112 due to being enrolled/dosed at two sites will be classified as "Significant" and "Exclude from all analyses sets". Biostatistics/Programming will exclude US3162112 from all analyses.

Sixth Instance: The same subject was enrolled at two sites

- Protocol deviation for US3562079 due to being enrolled/dosed at two sites will be classified as "Significant" and "Exclude from per-protocol analysis set only". Biostatistics/Programming will exclude US3562079 from per-protocol analyses.
- Protocol deviation for US3132036 due to being enrolled/dosed at two sites will be classified as "Significant" and "Exclude from all analyses sets". Biostatistics/Programming will exclude US3132036 from all analyses.

2. Dose Error Subjects who received incorrect treatment

	USUBJID	TRT01P	TRT01A	EXTRT	VISIT
1	mRNA-1273-P301-US309-2036	mRNA-1273	mRNA-1273	PLACEBO	Visit 2 Day 29
2	mRNA-1273-P301-US309-2037	Placebo	mRNA-1273	mRNA-1273	Visit 2 Day 29
3	mRNA-1273-P301-US311-2032	mRNA-1273	Placebo	PLACEBO	Visit 1 Day 1
4	mRNA-1273-P301-US311-2032	mRNA-1273	Placebo	PLACEBO	Visit 2 Day 29
5	mRNA-1273-P301-US315-2090	Placebo	mRNA-1273	mRNA-1273	Visit 1 Day 1
6	mRNA-1273-P301-US315-2090	Placebo	mRNA-1273	mRNA-1273	Visit 2 Day 29
7	mRNA-1273-P301-US316-2031	mRNA-1273	Placebo	PLACEBO	Visit 1 Day 1
8	mRNA-1273-P301-US316-2031	mRNA-1273	Placebo	PLACEBO	Visit 2 Day 29
9	mRNA-1273-P301-US316-2032	Placebo	mRNA-1273	mRNA-1273	Visit 1 Day 1
10	mRNA-1273-P301-US316-2032	Placebo	mRNA-1273	mRNA-1273	Visit 2 Day 29
11	mRNA-1273-P301-US324-2411	mRNA-1273	mRNA-1273	PLACEBO	Visit 2 Day 29
12	mRNA-1273-P301-US359-2034	mRNA-1273	mRNA-1273	PLACEBO	Visit 2 Day 29
13	mRNA-1273-P301-US359-2130	Placebo	mRNA-1273	mRNA-1273	Visit 2 Day 29
14	mRNA-1273-P301-US371-2291	Placebo	mRNA-1273	mRNA-1273	Visit 1 Day 1
15	mRNA-1273-P301-US371-2291	Placebo	mRNA-1273	mRNA-1273	Visit 2 Day 29
16	mRNA-1273-P301-US377-2010	Placebo	mRNA-1273	mRNA-1273	Visit 2 Day 29
17	mRNA-1273-P301-US381-2201	Placebo	mRNA-1273	mRNA-1273	Visit 2 Day 29
18	mRNA-1273-P301-US382-2324	mRNA-1273	Placebo	PLACEBO	Visit 1 Day 1
19	mRNA-1273-P301-US382-2324	mRNA-1273	Placebo	PLACEBO	Visit 2 Day 29

3.4 Use of Visit Windowing, Unscheduled Visits, and Record Selection

Was windowing used in one or more analysis datasets?

Yes, analysis is summarized by following analysis visit window for post injection assessments:

Step 1: If the assessments are collected at a scheduled visit, the collected data will be mapped to the nominal scheduled visit.

Step 2: If the assessments are collected at an unscheduled visit, the collected data will be mapped using the analysis visit windows described in Table X below. For subjects with confirmed COVID-19, unscheduled assessments will be preferably mapped to the visits with respect to the confirmation of COVID-19 (i.e. Illness Visit Day xx) over nominal scheduled visits (i.e. Day xx).

If a subject has multiple assessments within the same analysis visit, the following rule will be used:

- If multiple assessments occur within a given analysis visit, the assessment closest to the target study day will be used.
- If there are 2 or more assessments equal distance to the target study day, the last assessment will be used.

Table X Analysis Visit Window

Visit	**Target Study Day**	**Visit Window in Study Day**
Nasopharyngeal swab (or saliva)		

Visit	Target Study Day	Visit Window in Study Day
Day 1	1 (Date of First Injection)	1, Pre-first dose
Day 29		
Illness Visit Day 1	X (Date of NP Swab test)	X
Illness Visit Day 3	X+2	[X+1, X+2]
Illness Visit Day 5	X+4	[X+3, X+4]
Illness Visit Day 7	X+6	[X+5, X+6]
Illness Visit Day 9	X+8	[X+7, X+10]
Illness Visit Day 14	X+13	[X+11, X+16]
Illness Visit Day 21	X+20	[X+17, X+23]
Illness Visit Day 28	X+27	[X+24, X+34]
Vital Signs		
Day 1	1 (Date of First Injection)	1, Pre-first dose
Day 1	1 (Date of First Injection)	1, Post-first-dose
Day 29	29 (Date of Second Injection)	[2, 43] Pre-second-dose
Day 29	29 (Date of Second Injection)	[2, 43] Post-second dose
Day 57	57	[44, 88]
Day 119	119	[89, 164]
Day 209	209	[165, 301]
Day 394	394	[302, 576]
Day 759	759	[577, 773]
Illness Visit Day 1	X (Date of COVID-19 Confirmation)	X
Illness Visit Day 28	X+27	[X+2, X+34]
Immunogenicity		
Day 1	1	1, Pre-first dose
Day 29	29 (Date of Second Injection)	[23, 36] Pre-second-dose
Day 57	57	[44, 133]
Day 209	209	[134, 301]
Day 394	394	[302, 576]
Day 759	759	[577, 773]
Illness Visit Day 1	X (Date of NP Swab test)	X
Illness Visit Day 28	X+27	[X+2, X+34]

For the 2nd dosing planned for Day 29, a window of day [22, 43] is applied to decide if the 2nd dosing is received as per protocol, used as a condition for deriving per-protocol set.

3.5 Imputation/Derivation Methods

If date imputation was performed, were there rules that were used in multiple analysis datasets?

Yes, per statistical analysis, following incomplete/missing data have been imputed

- Imputation rules for missing dates of prior/concomitant medications, non-study vaccinations and procedures are provided in Appendix A.
- Imputation rules for missing AE dates are provided in Appendix B.
- If the biomarker results are reported as below the LLOQ or contains "<", the numeric values will be substituted by 0.5 × LLOQ in the summary. If the biomarker results contain ">" then the numeric values of ULOQ will be substituted.

4. Analysis Data Creation and Processing Issues

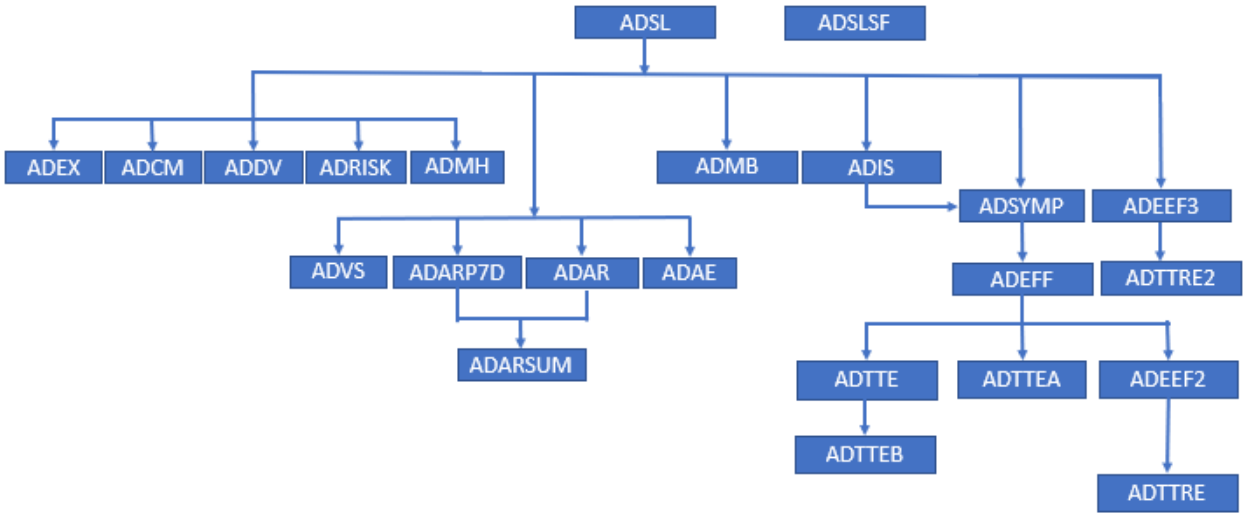
4.1 Split Datasets

ADAR.xpt (Solicited AR Analysis Dataset) has been split to ADAR1.xpt and ADAR2.xpt

ADAR1.xpt include all data where PARCAT1 = 'LOCAL'

ADAR2.xpt includes all data where PARCAT1 = 'SYSTEMIC'

4.2 Data Dependencies



4.3 Intermediate Datasets

No intermediate datasets have been created for BLA Interim Analysis

5. Analysis Dataset Descriptions

5.1 Overview

Are data for screen failures, including data for run-in screening (for example, SDTM values of ARMCD='SCRNFAIL', or 'NOTASSGN', or Null) included in ADaM datasets?

Screen failure data will not be included in analysis data sets except the subject level data could be found from ADaM.ADSLSF. All other screen failure data are included in SDTM

Are data taken from an ongoing study?

Yes, the study is still ongoing

Do the analysis datasets support all protocol and statistical analysis plan-specified objectives?
Yes

5.2 Analysis Datasets

Dataset - Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK /PD	Primary Objective	Structure
ADSL - Subject-Level Analysis Dataset	SUBJECT LEVEL ANALYSIS DATASET	X	X	X		X	One record per subject
ADAE - Adverse Event Analysis Dataset	OCCURRENCE DATA STRUCTURE		X			X	One record per subject per adverse event
ADAR - Solicited AR Analysis Dataset	BASIC DATA STRUCTURE		X			X	One record per subject, per parameter, per analysis timepoint
ADARP7D - Solicited AR post D7 Analysis Dataset	BASIC DATA STRUCTURE		X			X	One record per subject, per parameter, per analysis timepoint
ADARSUM - Solicited AR Summary Analysis Dataset	BASIC DATA STRUCTURE		X			X	One record per subject, per summary parameter, per analysis timepoint
ADCM - Concomitant Medication Analysis Dataset	OCCURRENCE DATA STRUCTURE		X	X			One record per subject per medication
ADDV - Deviation Analysis Dataset	OCCURRENCE DATA STRUCTURE			X			One record per subject per deviation

Dataset - Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK /PD	Primary Objective	Structure
ADEFF - Efficacy Analysis Dataset	BASIC DATA STRUCTURE	X				X	One record per subject, per parameter, per analysis timepoint
ADEFF2 - BOD/BOI Score Analysis Dataset	BASIC DATA STRUCTURE	X					One record per subject, per parameter, per time range
ADEFF3 - Symptom Score Analysis Dataset	BASIC DATA STRUCTURE	X					One record per subject, per parameter, per analysis timepoint
ADEX - Treatment Exposure Analysis Dataset	OCCURRENCE DATA STRUCTURE			X			One record per subject per administration
ADIS - Immunogenicity Analysis Dataset	BASIC DATA STRUCTURE	X*					One record per subject, per parameter category, per parameter, per assessment
ADMB - Microbiology Analysis Dataset	BASIC DATA STRUCTURE	X				X	One record per subject, per parameter, per analysis timepoint
ADMH - Medical History Analysis Dataset	OCCURRENCE DATA STRUCTURE			X			One record per subject per medical history

Dataset - Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK /PD	Primary Objective	Structure
ADRISK - Risk of Exposure Analysis Dataset	BASIC DATA STRUCTURE			X			One record per subject, per parameter
ADSLSF - Screen Fail Subj-Level Analysis Dataset	SUBJECT LEVEL ANALYSIS DATASET			X			One record per screen failed subject
ADSYMP - COVID-19 Symptom Analysis Dataset	BASIC DATA STRUCTURE	X				X	One record per subject, per parameter, per analysis timepoint
ADTTE - Time to Event Analysis Dataset	BASIC DATA STRUCTURE	X				X	One record per subject, per parameter
ADTTEA - Time to Adjudication Event Analysis Data	BASIC DATA STRUCTURE	X				X	One record per subject, per parameter
ADTTEB - Time to Event up to PDV Analysis Data	BASIC DATA STRUCTURE	X				X	One record per subject, per parameter
ADTTRE - Recurrent of BOD/BOI Analysis Dataset	BASIC DATA STRUCTURE	X					One record per subject, per parameter

Dataset - Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK /PD	Primary Objective	Structure
ADTTRE2 - Recurrent of Symptom Analysis Dataset	BASIC DATA STRUCTURE	X					One record per subject, per parameter, per event occurrence
ADVS - Vital Signs Analysis Dataset	BASIC DATA STRUCTURE		X				One record per subject per parameter per assessment

5.2.1 ADSL - Subject-Level Analysis Dataset

In addition to supporting all analyses, ADSL contains variables to also support baseline characteristics and disposition analyses. The population indicator variables are defined in ADSL and copied into other analysis datasets as needed. All subjects in DM, except for screen failures, were included in ADSL.

5.2.2 ADAE - Adverse Event Analysis Dataset

SDTM.AE contains unsolicited adverse events and solicited adverse reaction events (AR) if A solicited adverse reaction event was captured in adverse event form due to following reasons:

a. AR event is a serious event (AESER=Y)
b. AR event was last beyond day 7 after each vaccination reference date (MRDSTDY<=7 and MRDETDY>=8)

ADAE removed records from SDTM.AE if events were captured in AE due to a subject failed to report AR event via e-Diary before e-diary window closed (SUPPAE.QVAL=Y where QNAM=REMOVEFL)

A set of ANLXXFL variables were created to indicate if an AR event is a continue, re-started, or delayed event (see Table 5.2.2)

Table 5.2.2

ANL01FL	Set to 'Y' if all the conditions below are met: 1. ARTERM in ('Pain', 'Erythema', 'Swelling', 'Underarm Gland Swelling or Tenderness') 2. MRDSTDY>=8
ANL02FL	Set to 'Y' if all the conditions below are met: 1. ANL01FL='Y' 2. MRDSTDY=8 3. Record(s) can be found where ARTERM=FACE.FAOBJ and MDOSREF = FACE.FATPTREF and FACE.FATPTNUM =7 and FAORRES ne "NONE" or Missing by SUBJID
ANL03FL	Set to 'Y' if all the conditions below are met: 1. ANL01FL='Y' 2. Record(s) can been found from SDTM.FACE where ARTERM=FACE.FAOBJ and MDOSREF = FACE.FATPTREF and FAORRES ne "NONE" and not missing by SUBJID 3. No FACE.FATPT=7 and MRDSTDY=8 case can be found
ANL04FL	Y if all the conditions below are met: 1. ANL01FL='Y' 2. MRDSTDY>=8 2. Record(s) can not been found from SDTM.FACE where ARTERM=FACE.FAOBJ and MDOSREF = FACE.FATPTREF and FAORRES ne "NONE" and not missing by SUBJID

A set of SMQXXFL is based on 'Narrow' scope except anaphylactic reaction SMQ (SMQ01FL)

5.2.3 ADAR - Solicited AR Analysis Dataset

ADAR contains symptom data that are derived from SDTM.FACE (Daily Symptom within 7 days after each vaccine) and SDTM.VS (Fever if VS.ATPT<=7). It is based on one record per subject (SUBJID), per symptom (PARAMCD), per timepoint (ATPT), per vaccine reference (ATPTREF), per evaluator (FAEVAL = ' STUDY SUBJECT' or 'INVESTIGATOR' if data source is from FACE). Pooled Analysis Timepoint Variable (ATPTGR1) is created to set worse ATOXGR flag (ANL01FL) per subject, per symptom, per vaccination (Table 5.2.3 screen captured sample data).

Table 5.2.3

SUBJID	ATPT	ATPTREF	ATPTGR1	PARAMCD	ATOXGR	FAEVAL	ANL01FL
US3042111	DAY 1, 30 MINUTES AFTER VACCINATION (AT STUDY CLINIC)	Vaccination 2	**DAY1**	PAIN	GRADE 0	STUDY SUBJECT	
US3042111	DAY 1, AFTER VACCINATION (AT HOME)	Vaccination 2	**DAY1**	PAIN	GRADE 1	INVESTIGATOR	
US3042111	DAY 1, AFTER VACCINATION (AT HOME)	Vaccination 2	**DAY1**	PAIN	GRADE 1	STUDY SUBJECT	**Y**
US3042111	DAY 2	Vaccination 2	**DAY 2**	PAIN	GRADE 1	STUDY SUBJECT	
US3042111	DAY 2	Vaccination 2	**DAY 2**	PAIN	GRADE 2	INVESTIGATOR	**Y**

5.2.4 ADARP7D - Solicited AR post D7 Analysis Dataset

ADARP7D has the same data structure as ADAR, data are derived from SDTM.FACE (Daily Symptom within 7 days), SDTM.FAAE (Daily Symptom last and beyond day 7) and SDTM.VS. Data from SDTM.FACE are copied to ADARP7D if the same subject and symptom records (Toxicity Grade >0) are found from SDTM.FAAE (see table 5.2.4.1).

Table 5.2.4.1

STUDYID	USUBJID	ATPTREF	ATPT	PARAM	ATOXGR
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 1, AFTER VACCINATION (AT HOME)	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 2	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 3 **Source data is from FACE**	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 4	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 5	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 6	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 8	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 9 **Source data is from FAAE**	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 10	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 19	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 20	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 21	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 22	Erythema Longest Diameter (mm)	Grade 2
mRNA-1273-P301	mRNA-1273-P301-US316-2033	Vaccination 1	DAY 23	Erythema Longest Diameter (mm)	Grade 2

A set of records selection flag variables are created to support different analysis (see table 5.2.4.2)

Table 5.2.4.2

ANL01FL	Y for the records where PARAMCD is 'PAIN' or 'ERYTHDIA' or 'SWELLDIA', or 'LYMPH'
ANL02FL	If ANL01FL=Y, per subject per vaccination per symptom, flag all records if there are records at both ATPTN = 7 and ATPTN = 8.
ANL03FL	If ANL01FL=Y, per subject per vaccination per symptom with min(ATPTN) <=7, flag all records if there are not records at both ATPTN = 7 and ATPTN = 8.
ANL04FL	Y for the records if both criteria met: 1. ANL01FL='Y'; 2. If per subject per symptom (PARAMCD) per vaccination (ATPTREF), the smallest ATPTGR1N >=8
ANL05FL	Y for the first record with maximum non-missing ATOXGRN per subject per PARAM per vaccination (ATPTREF) per ATPT, i.e., the first available record per day. If there is two records per day and one from investigor and one from subject, select the one from subject (FAEVAL='STUDY SUBJECT' or missing FAEVAL for FEVER)
ANL06FL	per subject per vaccination per symptom, flag all records if the smallest ATPTGR1N<8 and largest ATPTGR1N>=8 where ATOXGRN>0

	Symptom Occured within 7 Day							Symptom Occurred after Day 7							
	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	
Case 1							X	X							ANL02FL=Y
Case 2							X		X						ANL03FL=Y
Case 2						X		X							
Case 2						X			X						
Case 3									X						ANL04FL=Y
Case 3								X	X						

5.2.5 ADARSUM - Solicited AR Summary Analysis Dataset

ADARSUM includes summary data of ADAR and ADARP7D. They contain

a. Topline symptom grade within 7 days after each vaccine that is derived from ADAR. One record per subject (SUBJID), per symptom (PARAMCD), worse grade (ATOXGR)and per vaccine from Day 1 to Day 7 (ATPTREF),

b. Total number of days with symptom grade > 0 that are derived from both ADAR and ADARP7D. One record per subject (SUBJID), per symptom(PARAMCD), and per vaccine (ATPTREF)

5.2.6 ADEFF - Efficacy Analysis Dataset

ADEFF contains COVID-19 cases that are derived from SDTM.MB, SDTM.CE (where CE.CECAT="ADJUDICATION"), SDTM.AE (where AESDTDH='Y' and SUPPAE.QVAL=Y and SUPPAE.QNAM='AECVDIAG'), ADSYMP and ADIS based on cases as defined in the SAP. It is based on one record per subject (SUBJID), per date (RT-PCR Test Date) of documented COVID-19 case that is created only if the case definition criteria met. Flag first record (ANL01FL = Y) per subject (SUBJID), per parameter (PARAMCD). that is used for ADTTE and ADTTEA

5.2.7 ADEFF2 - BOD/BOI Score Analysis Dataset

ADEFF2 contains score data of Burden of Disease (BOD)/ Burden of Infection (BOI) that support exploratory analysis of Burden of Disease (BOD) and Burden of Infection (BOI). Score data are derived from ADaM.ADEFF (see Table 5.2.7.1 for BOD score definition and Table 5.2.7.2 for BOI score definition).

Table 5.2.7.1

Participant Status (Worse Category Following Disease Detection)	BOD Score
Without COVID-19 (Uninfected/Asymptomatic Infection)	0
COVID-19 without Hospitalization (Symptomatic without Hospitalization)	1
COVID-19 with Hospitalization	2
Death	3

Table 5.2.7.2

Participant Status (Worse Category Following Disease Detection)	BOI Score
No Infection	0
Asymptomatic	1/2
COVID-19 without Hospitalization (Symptomatic without Hospitalization)	1
COVID-19 with Hospitalization	2
Death	3

5.2.8 ADEFF3 - Symptom Score Analysis Dataset

ADEFF3 contains grading of COVID-19 symptoms that support exploratory analysis of Vaccine Efficacy on Duration and Presence/Severity of COVID-19 Symptoms (see Table 5.2.8 for mapping between grading of COVID-19 symptoms and score).

Table 5.2.8

Grading	All Symptoms	For Nausea/Vomiting ONLY	For Sense of Smell / Taste ONLY	Score
None	No symptom			0
Mild	I had the symptom, but I could still do my normal activities	I was able to eat and drink normally	I had the symptom, but I retained some taste/smell	1
Moderate	The symptom really bothered me. It was hard to do my normal activities.	It bothered me enough that I did not eat or drink normally.	My taste/smell was significantly affected.	2
Severe	The symptom was very bad. I was not able to do activities that I usually do.	I could not eat or drink.	I have no taste or smell.	3

5.2.9 ADIS - Immunogenicity Analysis Dataset

ADIS contains immunogenicity data that is derived from SDTM.IS. It is based on one record per subject (SUBJID), per parameter (PARAMCD) and per timepoint (AVISIT). It was created to support Binding/Neutralized Antibody analyses Log10 transformed parameters were derived to support GMT and GMFR.

Positive serology test result (PARAMCD='SARSCOV2') based on bAb specific to SARS-CoV-2 nucleocapsid protein is one of key criteria for Asymptomatic SARS-CoV-2 Infection case.

5.2.10 ADMB - Microbiology Analysis Dataset

ADMB contains both RT-PCR test results and other microbiology data that is derived from SDT.MB. It is based on one record per subject (SUBJID), per parameter (PARAMCD) and per timepoint (AVISIT).

5.2.11 ADSYMP - COVID-19 Symptom Analysis Dataset

ADSYMP contains COVID symptom data derived from SDTM.FAEF, SDTM.PR, SDTM.HO (where HOCAT='EFFICACY') and SDTM.VS (where VS.VSCAT='EFFICACY'). It is based on one record per subject (SUBJID), per symptom (PARAMCD), per assessment timepoint. Symptom assessment date (ADT) is derived from SDTM.--DTC (--: FAEF, PR, HO and VS) regardless symptom occurred, Symptom start date (ASTDT) is derived from --STDTC or SUPPFAEF.FAEVDTC (--: HO or PR) that is captured from Severe COVID-19 form only.

5.2.12 ADTTE - Time to Event Analysis Dataset

ADTTE contains SAP defined time to COVID-19 event data that is derived from ADEFF where PARCAT1 = 'Derived Per SAP'. It is based on one record per subject (SUBJID), per type of time to event parameter (PARAMCD).

Please note the ADTTE.PARAMCD TTINFx, TTASYMPx and TTASYCRx are not used in analysis of SARS-CoV-2 Infection Regardless of Symptomatology or Severity, or Asymptomatic Infection, respectively. Please refer to Section 5.2.14 on ADTTEB for additional information.

5.2.13 ADTTEA - Time to Adjudication Event Analysis Data

ADTTEA contains adjudicated time to COVID-19 event data that is derived from ADEFF where PARCAT1 = 'Derived Per Adjudication'. It is based on one record per subject (SUBJID), per type of time to event parameter (PARAMCD).

5.2.14 ADTTEB - Time to Event up to PDV Analysis Data

ADTTEB contains time to event including to PDV (Participant Decision Visit) data that is derived from ADEFF where PARCAT1 = 'Derived per SAP'. It is based on one record per subject (SUBJID), per type of time to event parameter (PARAMCD).

ADTTEB is used for analysis of SARS-CoV-2 Infection Regardless of Symptomatology or Severity (PARAMCD in TTINFBx), and Asymptomatic Infection (PARAMCD in TASYCRBx using competing risk), and results of these analyses are included in CSR.

6. Data Conformance Summary

6.1 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**
If yes, describe any significant sponsor-defined validation rules:	**n/a**
(Text or table here. If significant amount, include as an appendix)	
Were the ADaM datasets evaluated in relation to define.xml?	**Yes**
Was define.xml evaluated?	**Yes**

Provide any additional compliance evaluation information:

ADaM dataset time stamps are after TFL creation time. This is because ADaM datasets have been rerun due to update ADaM programs by

- Removing unused variables (COMPLFL, RIG1DFL, RIGYAFL, COP1FL, COP2FL and IGSFL) from CORE variables
- Removing unused data from ADaM.ADTTE :
  TTCVD1-6 (COVID-19 without censoring of prior infection)
  TTCVDSE1-6 (severe COVID-19 without censoring of prior infection)
  TTCVDSD1-6 (2nd definition of COVID-19 without censoring of prior infection)
- Removing unused data from ADaM.ADTTEA:
  TTCVD1-6 (COVID-19 without censoring of prior infection)
  TTCVD1B (COVID-19 up to 53rd case without censoring of prior infection)
  TTCVDSE1-6 (severe COVID-19 without censoring of prior infection)
  TTASYMP1-6 (asymptomatic infection censored by adjudicated COVID-19)

6.2 Issues Summary

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
AD0019	COMPLFL subject-population flag value is null	Error	ADSL	27588 (90.68%)	This is due to study is still ongoing
AD0196	Required SEX value is null	Error	ADSL	1 (< 0.1%)	Data collection issue due to the study status is still ongoing
AD0253	Record key from SDTM AE is not traceable to ADaM ADAE (not enough ADAE recs)	Error	AE	1459 (3.72%)	Any solicited AR captured in AE form has been moved to either ADAR (within 7 days after each vaccine) or ADARP7D (last or after 7 days after each vaccine) unless it meets the criteria for SAE or lasts beyond 7 days post injection, but SDTM.AE is flagged such record as SUPPAE.REMOVEFL=Y instead of remove
AD0279	ASEVN value != 1, 2, 3, or null	Error	ADAE	562 (1.49%)	Per protocol, AR analysis is based both AESEV and AETOXGR, ASEV is created for such type analysis
AD0304	Only some of these variables are present and populated: SMQ11NAM,SMQ11CD,SMQ11SC	Error	ADAE	485 (100.00%)	SMQXXCD is permissible variable, accept current setting

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
AD0304	Only some of these variables are present and populated: SMQ09NAM,SMQ09CD,SMQ09SC	Error	ADAE	62 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ02NAM,SMQ02CD,SMQ02SC	Error	ADAE	375 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ01NAM,SMQ01CD,SMQ01SC	Error	ADAE	2012 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ14NAM,SMQ14CD,SMQ14SC	Error	ADAE	613 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ10NAM,SMQ10CD,SMQ10SC	Error	ADAE	148 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ06NAM,SMQ06CD,SMQ06SC	Error	ADAE	1462 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ12NAM,SMQ12CD,SMQ12SC	Error	ADAE	33 (100.00%)	SMQXXCD is permissible variable, accept current setting

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
AD0304	Only some of these variables are present and populated: SMQ04NAM,SMQ04CD,SMQ04SC	Error	ADAE	17 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ03NAM,SMQ03CD,SMQ03SC	Error	ADAE	1657 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ08NAM,SMQ08CD,SMQ08SC	Error	ADAE	2 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ05NAM,SMQ05CD,SMQ05SC	Error	ADAE	13 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ07NAM,SMQ07CD,SMQ07SC	Error	ADAE	231 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ13NAM,SMQ13CD,SMQ13SC	Error	ADAE	72 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ01NAM,SMQ01CD,SMQ01SC	Error	ADMH	3399 (100.00%)	SMQXXCD is permissible variable, accept current setting

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
AD0304	Only some of these variables are present and populated: SMQ02NAM,SMQ02CD,SMQ02SC	Error	ADMH	6405 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0304	Only some of these variables are present and populated: SMQ06NAM,SMQ06CD,SMQ06SC	Error	ADMH	20187 (100.00%)	SMQXXCD is permissible variable, accept current setting
AD0366B	RANDFL value is not Y, when RANDDT is populated	Error	ADSL	8 (< 0.1%)	These are enrollment issues that already added explanations to Reviewer's Guide in the details
AD1012	Secondary custom variable is present, but its primary variable is not present	Warning	ADEFF3	2 (22.22%)	Misleading validation message
AD1012	Secondary custom variable is present, but its primary variable is not present	Warning	ADMH	3 (33.33%)	False positive message
AD1019	Illegal variable name: xx is not in [01-99] for an ADSL trial date	Error	ADSL	4 (25.00%)	APXXSSDT and APXXENDT are safety reference date, accepted.
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADAR	206913 (4.09%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADARP7D	6776 (5.35%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADARSUM	44844 (4.20%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADCM	7593 (3.89%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADDV	3063 (3.73%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADEFF	917 (5.07%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADEFF2	21714 (4.05%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADEFF3	14010 (4.56%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADEX	3484 (4.09%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADIS	10561 (4.04%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADMB	10167 (4.81%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADMH	5671 (3.21%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADRISK	23427 (4.06%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADSL	1234 (4.06%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADSYMP	56447 (5.34%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADTTE	61739 (4.06%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADTTEA	16938 (4.06%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADTTEB	12310 (4.06%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADTTRE	2501 (4.05%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADTTRE2	75 (3.80%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
CT2002	RACE value not found in 'Race' extensible codelist	Warning	ADVS	48729 (4.06%)	RACE = "MULTIPLE" because patient checked more than one race. RACE = "OTHER" because data was captured from CRF
SD0037	Value for PARAM not found in (BOD/BOI Score Analysis Parameter Code) user-defined codelist	Error	ADEFF2	536274 (100.00%)	Compared PARAMCD/PARAM listing between ADEFF2 and define.xml and did not find any missing terms.
SD0037	Value for PARAM not found in (Symptom Score Analysis Parameter Code) user-defined codelist	Error	ADEFF3	307100 (100.00%)	Compared PARAMCD/PARAM listing between ADEFF3 and define.xml and did not find any missing terms.
SD0037	Value for PARAM not found in (Immunogenicity Analysis Dataset Parameter Code) user-defined codelist	Error	ADIS	261357 (100.00%)	Compared PARAMCD/PARAM listing between ADIS and define.xml and did not find any missing terms.
SD0037	Value for PARAM not found in (Time to Event Analysis Data Set Parameter Code) user-defined codelist	Error	ADTTE	1522428 (100.00%)	Compared PARAMCD/PARAM listing between ADTTE and define.xml and did not find any missing terms.
SD0037	Value for PARAM not found in (Time to Adjudication Event Analysis Data Set Parameter Code) user-defined codelist	Error	ADTTEA	417706 (100.00%)	Compared PARAMCD/PARAM listing between ADTTEA and define.xml and did not find the miss-match and will discuss with Pinnacle 21 expert to understand the checking logic. There is no impact for first interim analysis

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD0037	Value for PARAM not found in (Time to Event up to PDV Analysis Data Set Parameter Code) user-defined codelist	Error	ADTTEB	303460 (100.00%)	Compared PARAMCD/PARAM listing between ADTTEB and define.xml and did not find any missing terms.
SD1071	Dataset is greater than 5 GB in size	Warning	ADAR	1 (100.00%)	Split ADAR1.sas7bdat and ADAR2.sas7bdat are included in split folder
DD0006	Missing required 'Description' value	Error	DEFINE	2 (100.00%)	False positive message
DD0099	Extended value for AnalysisReason	Warning	DEFINE	2 (100.00%)	False positive message
DD0100	Extended value for AnalysisPurpose	Warning	DEFINE	2 (100.00%)	False positive message

7. Submission of Programs

All programs for analysis datasets and primary and secondary efficacy results are submitted. They were all created on a SAS Server platform using V9.4. The internal reference date used to create dates in ADaM datasets is 2020-05-04

7.1 ADaM Pprograms

Program Name	Output	Macro Used
A10ADSL.TXT	ADSL.SAS7BDAT	MADAM
A11ADSLSF.TXT	ADSLSL.SAS7BDAT	MADAM
A20ADAE.TXT	ADAE.SAS7BDAT	MADAM
A20ADAR.TXT	ADAR.SAS7BDAT	MADAM
A20ADARP7D.TXT	ADARP7D.SASBDAT	MADAM
A30ADARSUM.TXT	ADARSUM.SAS7BDAT	MADAM
A20ADCM.TXT	ADCM.SAS7BDAT	MADAM
A20ADEX.TXT	ADEX.SAS7BDAT	MADAM
A20ADDV.TXT	ADDV.SAS7BDAT	MADAM
A20ADIS.TXT	ADIS.SAS7BDAT	MADAM
A20ADMB.TXT	ADMB.SAS7BDAT	MADAM
A20ADMH.TXT	ADMH.SAS7BDAT	MADAM
A20ADRISK.TXT	ADRISK.SAS7BDAT	MADAM
A20ADVS.TXT	ADVS.SAS7BDAT	MADAM
A20ADSYMP.TXT	ADSYMP.SAS7BDAT	MADAM

Program Name	Output	Macro Used
A40ADEFF.TXT	ADEFF.SAS7BDAT	MADAM
A50ADEFF2.TXT	ADEFF2.SAS7BDAT	MADAM
A50ADEFF3.TXT	ADEFF3.SAS7BDAT	MADAM
A50ADTTE.TXT	ADTTE.SAS7BDAT	MADAM
A50ADTTEA.TXT	ADTTEA.SAS7BDAT	MADAM
A60ADTTRE.TXT	ADTTRE.SAS7BDAT	MADAM
A60ADTTRE2.TXT	ADTTRE2.SAS7BDAT	MADAM

7.2 Analysis Output Programs

Program Name	Output Number	Title	Input
T140301010101.TXT	Table 14.3.1.1.1.1	Summary of Subjects with Solicited Adverse Reactions Within 7 Days After First Injection by Grade, First Injection Solicited Safety Set	ADSL, ADAR
T140301070101.TXT	Table 14.3.1.7.1.1	Summary of Unsolicited TEAE up to 28 Days After Any Injection Safety Set	ADSL, ADAE
T14020201030101.TXT	Table 14.2.2.1.3.1.1	Analysis of Vaccine Efficacy of mRNA-1273 to Prevent COVID-19* Based on Adjudication Committee Assessments Starting 14 Days After Second Injection Per-Protocol Set	ADSL, ADTTEA

Program Name	Output Number	Title	Input
T1402040101010301.TXT	Table 14.2.4.1.1.1.3.1	Summary of Binding Antibody Specific to SARS-CoV-2 Spike Protein by MSD by Baseline SARS-CoV-2 Status Per-Protocol Random Sub-cohort for Immunogenicity	ADSL, ADIS

7.3 Macro programs

Program Name	Purpose
MADAM	Derive record level treatment variables: TRTA and TRTAN Derived baseline flag and analysis window variables: ABLFL, AVISIT, AWRANGE, AWTARGET Derive analysis change and % of change variables: CHG, and PCHG Derive dose reference and reference date variables: XXDOSREF and XXRDDY Derive record stage and phase variables, Stage and Phase Derive analysis date and day variables: ASTDT, AENDT, ASDY, AEDY
MARTZ_DEFAULT	Define Study Level ArtZ Defaults
MCLOPPER	Create Inferential Statistical Analysis Macro: rate ratio of SAR and 95% CI.
MCLOPPERIS	Create Inferential Statistical Analysis Macro: seroresponse and x-fold increase from baseline in summary of immunogenicity.
MGM_CI	Create Inferential Statistical Analysis Macro: geometric mean level/titer or geometric mean fold rise, and 95% CI.
MT1403010101_SAR_BYGRADE	Create common code - Table Summary of Solicited Adverse Reactions by Grade
MT1403010701_AE	Create common code - Table Summary of Unsolicited TEAE
MT140202010101_VE	Macro to create vaccine efficacy tables. No output and title.
MT140204010101010X	Create common code - Table Summary of Binding Antibody Specific to SARS-CoV-2 Spike Protein by MSD by Baseline Elecsys Result
MVEHRIR	Create Inferential Statistical Analysis: vaccine efficacy based on hazard ratio or incidence rate, and 95% CI.

8. Appendix

Appendix A Imputation Rules for Missing Dates of Prior/Concomitant Medications and Non-Study Vaccinations

Imputation rules for missing or partial start/stop dates of medication are defined below:

1. Missing or partial medication start date:
   - If only Day is missing, use the first day of the month, unless:
     - The medication end date is on/after the date of first injection or is missing/partial AND the start month and year of the medication coincide with the start month and year of the first injection. In this case, use the date of first injection.
   - If Day and Month are both missing, use the first day of the year, unless:
     - The medication end date is on/after the date of first injection or is missing/partial AND the start year of the medication coincide with the start year of the first injection. In this case, use the date of first injection.
   - If Day, Month, and Year are all missing, the date will not be imputed, but the medication will be treated as though it began prior to the first injection for purposes of determining if status as prior or concomitant.
2. Missing or partial medication stop date:
   a. If only Day is missing, use the earliest date of (last day of the month, study completion, discontinuation from the study, or death).
   b. If Day and Month are both missing, use the earliest date of (last day of the year, study completion, discontinuation from the study, or death).
   c. If Day, Month, and Year are all missing, the date will not be imputed, but the medication will be flagged as a continuing medication.

In summary, the prior, concomitant or post categorization of medications and non-study vaccinations is described in Table A below.

Table A Prior, Concomitant, and Post Categorization of Medications and Non-study Vaccinations

Medication Start Date	Medication Stop Date		
	< First Injection Date of IP	= First Injection Date and = 28 Days After Last Injection	> 28 Days After Last Injection [2]
< First injection date of IP [1]	P	P, C	P, C, A
= First injection date and = 28 days after last injection	-	C	C, A
> 28 days after last injection	-	-	A

A: Post; C: Concomitant; P: Prior

[1] includes medications with completely missing start date

[2] includes medications with completely missing end date

Appendix B Imputation Rules for Missing Dates of AEs

Imputation rules for missing or partial start dates and stop dates of AEs are defined below:

1. Missing or partial start date:

- If only Day is missing, use the first day of the month, unless:
  - The AE end date is on/after the date of first injection or is missing/partial AND the start month and year of the AE coincide with the start month and year of the first injection. In this case, use the date and time of first injection, even if AE time was collected.
- If Day and Month are both missing, use the first day of the year, unless:
  - The AE end date is on/after the date of first injection or is missing/partial AND the start year of the AE coincides with the start year of the first injection. In this case, use the date and time of first injection, when time is available.
- If Day, Month, and Year are all missing, the date will not be imputed. However, if the AE end date is prior to the date of first injection, then the AE will be considered a pre-treatment AE. Otherwise, the AE will be considered treatment-emergent.

2. Missing or partial end dates will not be imputed.