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Clinical Study Data Reviewer's Guide for Sequencing Data Analysis

BLA Analysis for Participants ≥16 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 for Sequencing data Analysis	03-Jun-2021

Clinical Study Data Reviewer's Guide

Contents

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. This cSDRG is a supplement to the primary cSDRG previously submitted for the BLA and covers only the efficacy sequencing data analyses in the blinded placebo-controlled follow-up period for the COVID-19 case data (cutoff date:13Mar2021)

1.2 Acronyms

Acronym	Translation
COVID-19	Coronavirus Disease 2019
cSDRG	Clinical Study Data Reviewer's Guide
SDTM	Study Data Tabulation Model
BLA	Biologics Licensing Application

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

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Standard or Dictionary	Versions Used
Medications Dictionary	WHODD GLOBALV3Mar20, WHO DDE v202003, SNOMED 2020-09-01, UNII 2020-08-18, NDF-RT 2020-09-08

2. Protocol Description

2.1 Protocol Number and Title

Refer to the primary cSDRG.

2.2 Protocol Design

Refer to the primary cSDRG.

2.3 Trial Design Datasets

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

Refer to the primary cSDRG for complete details of the trial design datasets

3. Subject Data Description

3.1 Overview

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

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

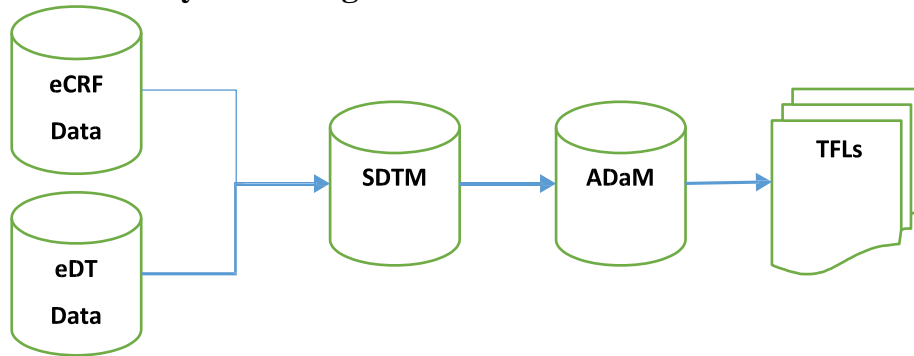Do the submission datasets include screen failures? **Yes**

Refer to the primary cSDRG for further details

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.

Explanation of data fields [Not Submitted]

Refer to the primary cSDRG for further details.

3.4 SDTM Subject Domains

Only the domains relevant to the sequencing data analysis are listed below. DM and EX have been included in the package for Pinnacle checks and these domains are identical to the datasets included in the BLA esub package, for the list of complete domains refer to the primary cSDRG.

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Dataset - Dataset Label	Efficacy	Safety	Other	SUPP--	Related Using RELREC
XB - Sequencing Data	X				

3.4.1 XB – Sequencing Data

The XB domain is a custom domain and is similar to the MB domain. XB was created to support the sequencing data which is a distinct analysis separate from the primary analysis. Sequencing data dataset consists of one record per microbiology specimen finding per time point per visit per subject.

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 4.2.0**
                                              Validation Engine version 2010.1

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

    The issues for DM and EX are not included, only XB domain issues are listed below. Refer to the primary cSDRG for the issue summary of all the domains that are part of the primary submission.

Check ID	Diagnostic Message	FDA Severity	Dataset	Count (Issue Rate)	Explanation
SD1082	Variable length is too long for actual data	Error	XB	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. Pinnacle 21 provides false positive information since it only checks the length of the variable within the data set.
SD1203	XBDTC date is after RFPENDTC	Error	XB	2 (0.27%)	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.
CT2002	XBMETHOD value not found in 'Method' extensible codelist	Warning	XB	1146 (100.00%)	New terms were added to extensible codelist Method (C85492) for the study protocol needs: • Next generation sequence
CT2002	XBSPEC value not found in 'Specimen Type' extensible codelist	Warning	XB	1146 (100.00%)	New terms were added to extensible codelist Specimen Type (C78734) for the study protocol needs: • NASAL_SWAB • NASAL_SWAB_SELF
CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	XB	279 (24.35%)	New terms were added to extensible codelist EPOCH (C99079) for the study protocol needs: •VACCINATION •OPEN LABEL FOLLOW-UP •REPEAT SCREENING 1

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