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

<table>
<thead>
<tr>
<th>Version</th>
<th>Summary of Major Change(s) and Impact</th>
<th>Version Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>First approved version of Clinical Data Reviewer’s Guide for Sequencing data Analysis</td>
<td>03-Jun-2021</td>
</tr>
</tbody>
</table>
Clinical Study Data Reviewer’s Guide

Contents

Study C4591001 ................................................................................................................................. 1
Clinical Data Reviewer’s Guide Revision history ............................................................................... 2
1. Introduction .................................................................................................................................... 4
   1.1 Purpose ..................................................................................................................................... 4
   1.2 Acronyms .................................................................................................................................. 4
   1.3 Study Data Standards and Dictionary Inventory ......................................................................... 4
2. Protocol Description ...................................................................................................................... 5
   2.1 Protocol Number and Title ....................................................................................................... 5
   2.2 Protocol Design ....................................................................................................................... 5
   2.3 Trial Design Datasets .............................................................................................................. 5
3. Subject Data Description ............................................................................................................... 5
   3.1 Overview .................................................................................................................................. 5
   3.2 Traceability Flow Diagram ...................................................................................................... 5
   3.3 Annotated CRFs ....................................................................................................................... 6
   3.4 SDTM Subject Domains ........................................................................................................... 6
      3.4.1 XB – Sequencing Data ...................................................................................................... 7
4. Data Conformance Summary ........................................................................................................ 7
   4.1 Conformance Inputs ................................................................................................................ 7
   4.2 Issues Summary ....................................................................................................................... 7
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

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Translation</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19</td>
<td>Coronavirus Disease 2019</td>
</tr>
<tr>
<td>cSDRG</td>
<td>Clinical Study Data Reviewer’s Guide</td>
</tr>
<tr>
<td>SDTM</td>
<td>Study Data Tabulation Model</td>
</tr>
<tr>
<td>BLA</td>
<td>Biologics Licensing Application</td>
</tr>
</tbody>
</table>

1.3 Study Data Standards and Dictionary Inventory

<table>
<thead>
<tr>
<th>Standard or Dictionary</th>
<th>Versions Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDTM</td>
<td>• SDTM v1.4</td>
</tr>
<tr>
<td></td>
<td>• SDTM-IG v3.2</td>
</tr>
<tr>
<td>Controlled Terminology</td>
<td>CDISC SDTM Controlled Terminology, 2020-03-27</td>
</tr>
<tr>
<td>Data Definitions</td>
<td>Define-XML v2.0</td>
</tr>
</tbody>
</table>
### Standard or Dictionary

<table>
<thead>
<tr>
<th>Standard or Dictionary</th>
<th>Versions Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medications Dictionary</td>
<td>WHO/DD GLOBALV3Mar20, WHO DDE v202003, SNOMED 2020-09-01, UNII 2020-08-18, NDF-RT 2020-09-08</td>
</tr>
</tbody>
</table>

#### 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
![Flow Diagram]

- eCRF Data
- SDTM
- ADaM
- TFLs
- eDT Data

### 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.
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.
<table>
<thead>
<tr>
<th>Check ID</th>
<th>Diagnostic Message</th>
<th>FDA Severity</th>
<th>Dataset</th>
<th>Count (Issue Rate)</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD1082</td>
<td>Variable length is too long for actual data</td>
<td>Error</td>
<td>XB</td>
<td>1 (5.00%)</td>
<td>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.</td>
</tr>
<tr>
<td>SD1203</td>
<td>XBDTC date is after RFPENDTC</td>
<td>Error</td>
<td>XB</td>
<td>2 (0.27%)</td>
<td>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.</td>
</tr>
</tbody>
</table>
| 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 |