RESPONSE TO FDA COMMENTS ON CLINICAL RECEIVED ON 24 SEPTEMBER 2021

The Sponsor acknowledges FDA comments on CLINICAL topics (in **Bold)**

Our review of your August 24, 2021 submission (STN 125752/2) is ongoing. We have several requests for additional information regarding your datasets.

Priority Group # 3: Comments 12-17
Please respond to these comments by October 24, 2021. These comments pertain to the following:

1. **Clarifications**
2. **Inconsistent coding**
3. **Future improvements**
4. **Improper sub-categorizations**

ITEM 1:

12. **In AE, the subcategory 'PIMMC' is not useful as it is reported for most of the events that are categorized as AEs – e.g., upper respiratory infection, finger fracture, UTI, etc., and sometimes even reactogenicity events. Please correctly subcategorize these events in the future. If the event does not need a subcategory then AESCAT can be null. Please note that other subcategories that we are suggesting for AEs besides PIMMC is 'NOCD' and 'Exacerbation of a chronic disease.'**

Sponsor Response

The Sponsor appreciates the comment, agrees, and will update the mapping logics for AESCAT in future submissions.

ITEM 2:

13. Many event dates appear inconsistent between CE, FAEF, and SUPPFAEF. For example, subject 348-2303 reported Clinical and Radiographical Evidence of Pneumonia on 2021-01-14 in FAEF. However according to CE, both events started on 2021-01-21. In addition, a date of 2021-01-21 was recorded for both events in SUPPFAEF. Similarly, subject 334-2182 reported Clinical and Radiographical Evidence of Pneumonia on 2020-12-23 in FAEF, but both events were reported as having started on 2021-01-17 in CE. A date of 2021-01-17 was also recorded for these events in SUPFAEF. Please explain the discrepancies in the reported dates between these datasets.

Sponsor Response

In this study, surveillance for COVID-19 symptoms includes weekly telephone calls. COVID-19 symptoms and dates are collected in eCRF form "Covid-19 Severity Assessment". The start and

end dates of an event are mapped to SDTM FAEF domain variables FAEVDTC and FAENDTC (Display 1 and 2). Topline record event dates are mapped to CE domain variables CESTDTC and CEENDTC (Display 3).

In addition, in the raw data, there is a 'folder instance name' field that is consisted of both the eCRF form name and a date (Display 1: column 2). Such date is mapped to FA domain variable FADTC (Date/Time of Collection). Please note there is no standalone question on date of collection on the eCRF form "Covid-19 Severity Assessment", and there may be more than one symptom with specific/different start/end dates of each symptom collected with the same value of 'folder instance name' (please see row 2 of Display 1 on subject US3482302). The Sponsor also checked the eCRF form 'COVID-19 Contact', and in the raw date (Display 4), the dates of contact for these two subjects match the date part of 'folder instance name' field for these two subjects.

Display 1: Raw data from eCRF form: Covid-19 Severity Assessment

Subject name or identifier	Folder instance name	Clinical Evidence	Clinical Evidence Date of Assessment	Radiographical Evidence	Radiographical Date of Assessment	Oxygen Saturation (Character)	SPO2 Start Date
US3342182	Covid-19 Assessment 23 Dec 2020	Yes	1/17/2021	Yes	1/17/2021		
US3482302	Covid-19 Assessment 14 Jan 2021	Yes	1/21/2021	Yes	1/21/2021	86	1/20/2021

Display 2: SDTM FAEF /SUPPFAEF domains:

USUBJID	FATEST	FAOBJ	FACAT	FAORRES	FADTC	FAEVDTC	FAENDTC
mRNA-1273-P301-US334-2182	Occurrence Indicator	Clinical Evidence of Pneumonia	EFFICACY	Y	2020-12-23	2021-01-17	
mRNA-1273-P301-US334-2182	Occurrence Indicator	Radiographical Evidence of Pneumonia	EFFICACY	Y	2020-12-23	2021-01-17	
mRNA-1273-P301-US348-2302	Occurrence Indicator	Clinical Evidence of Pneumonia	EFFICACY	Y	2021-01-14	2021-01-21	
mRNA-1273-P301-US348-2302	Occurrence Indicator	Radiographical Evidence of Pneumonia	EFFICACY	Y	2021-01-14	2021-01-21	

FAEVDTC = Start Date/Time of Collection
FAENSTC = End Date/Time of Observation

Display 3: SDTM CE domain:

USUBJID	CETERM	CECAT	CEDTC	CESTDTC	CEENDTC
mRNA-1273-P301-US334-2182	Clinical Evidence of Pneumonia	EFFICACY	2021-01-17	2021-01-17	
mRNA-1273-P301-US334-2182	Radiographical Evidence of Pneumonia	EFFICACY	2021-01-17	2021-01-17	
mRNA-1273-P301-US348-2302	Clinical Evidence of Pneumonia	EFFICACY	2021-01-21	2021-01-21	
mRNA-1273-P301-US348-2302	Radiographical Evidence of Pneumonia	EFFICACY	2021-01-21	2021-01-21	

Display 4: Raw Data from eCRF form: COVID-19 Contact

Subject name or identifier	eCRF page name	Date of Contact	Type of Contact
US3342182	COVID-19 Contact	12/23/2020	Clinical Visit - Unscheduled
US3482302	COVID-19 Contact	1/14/2021	Clinic Visit - Scheduled

ITEM 3:

14. Medication provided to either prevent or treat solicited events should be reported in CM instead of or in addition to SUPPVS. Please ensure that any future datasets submitted will include this information in CM.

Sponsor Response

The sponsor acknowledges the comments. SUPPVS records for medication to either prevent or treat solicited events came from the "Yes /No" question on eDiary "Temperature_Day" which is solicited on a daily basis; no further information on the medication such as name of the medication, start or end date are captured. Therefore, we are unable to report in CM domain as more information would be required for records in CM domain.

ITEM 4:

15. It appears that you have summarized reactogenicity events in CE to include solicited events occurring within the 30 minutes to 1-hour post-vaccination time frame. Immediate solicited events should be reported in CE on a separate line from the Day 1-7 event and be categorized in CECAT as 'Immediate Reaction.' Please implement this in any future submissions.

Sponsor Response

The Sponsor would like to thank the reviewers for the comment and will implement the suggestion in future submissions. In P301, "immediate reaction" reflects solicited events occurring with 60 minutes. These information are available in FACE domain. In future submissions, an individual line will be added in CE domain with CECAT as "Immediate Reaction".

ITEM 5:

16. Inconsistent coding was used for the exact same AE and/or MH term (see table below for example). In the Reviewer's Guide you indicate that there is no issue due to inconsistent coding. We disagree with this assessment, as inconsistent coding can impact our safety analysis. In future submissions, please ensure that you provide data with consistent coding.

- 1 (distinct) AETERM

aeterm	aellt	aedecod	aehlt	aehlgt	aebodsys	count_of_aes	med drav
UPPER RESPIRATORY ILLINESS	UPPER RESPIRATORY DISORDER	RESPIRATORY DISORDER	RESPIRATORY TRACT DISORDERS NEC	RESPIRATORY DISORDERS NEC	RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	1	23
UPPER RESPIRATORY ILLINESS	UPPER RESPIRATORY INFECTION	UPPER RESPIRATORY TRACT INFECTION	UPPER RESPIRATORY TRACT INFECTIONS	INFECTIONS - PATHOGEN UNSPECIFIED	INFECTIONS AND INFESTATIONS	1	23

Sponsor Response

The inconsistency of the coded terms was not recognized prior to the data submission. The coding inconsistency was discovered by Moderna shortly after submission. A process for identifying coding inconsistencies prior to any data cuts or submissions has been implemented in order to recognize data inconsistencies during ongoing coding review and finalization.

ITEM 6:

17. With regards to ongoing solicited events, we had previously requested that reactogenicity events lasting beyond Day 7 and collected in the 'Medical Attention Day' Form be mapped to FACE for the day-to-day information instead of FAAE. For this submission, we will not request that you update the data in FACE with the data in FAAE; however, please ensure that reactogenicity events lasting beyond Day 7 and collected in the 'Medical Attention Day' Form are mapped to FACE for the dayto-day information instead of FAAE.

Sponsor Response

The Sponsor would like to thank the reviewers for your understanding and suggestions for future updates. The Sponsor would like to use this opportunity to clarify that, currently, for reactogenicity events lasting beyond Day 7, events on Day 1-7 are mapped to FACE; only events on Day 8 and beyond are mapped to FAAE, specifically, data collected in 'Medical Attention Day' form with MAAEFL="Y" is mapped to FAAE/SUPPFAAE by timepoint starting from 'Day 8'.

The Sponsor would like further clarification of the reviewers' request for future updates and would like to discuss this topic during the upcoming teleconference with the reviewers.