125752 Data validation Report Summary and Subsequent follow-up with Moderna

Our Reference: STN 125752 (studied under IND 19745, authorized under EUA 27073 on Dec 18, 2020)

Sponsor: Moderna

Product: COVID-19 Vaccine (Proposed tradename: Spikevax)

Proposed Indication: Active immunization in adults 18 years of age and older for the prevention of coronavirus disease-19.

On May 28, 2021, the sponsor submitted the beginning of the original rolling biologics license application. On August 24, 2021, they submitted the final part of the rolling submission which contained the datasets for two clinical trials:

- **mRNA-1273-P201** -phase 2a – initiated May 2020 – data lock Nov 5, 2020 (Part A (blinded) CSR primary analysis Day 57) - Randomized, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine (50 and 100 mcg) in Adults Aged 18 Years and Older
    - Part A addendum is provided with datasets in which the safety (adverse events [AEs] leading to discontinuation from study participation, medically attended AEs [MAAEs], serious AEs [SAEs], vital sign measurements, and assessments for SARS-CoV-2 infection) and immunogenicity (binding antibody and neutralizing antibody titer) results are presented through the Participant Decision Clinic Visit (database lock date of 10 Jun 2021). Participants were considered to have completed Part A of the study if they completed the final visit on Day 394 (Month 13) or initiated Part B [booster?] (from Participant Decision Clinic Visit) of the study.
- **mRNA-1273-P301** – phase 3 – initiated July 27, 2020 – Dec 2020 (First participant decision visit) - Mar 26, 2021 (data cutoff date) – database lock on May 4, 2021 - 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. Part A is the blinded phase and part B is the open label.

On September 10, 2021, the eDATA team discussed the validation results with the review committee for STN 125752/0. Based on the validation results of the datasets for P301 (beginning page 9 below) and a deeper dive into the datasets, the following concerns were identified (most of these concerns should also be relevant for P201):

- The SDTM define file stylesheet has an incorrect filename ('define1-0-0.xsl'). They need to change to 'define2-0-0.xsl' and resubmit to enable us to view define.
- Inconsistent coding was used for the exact same AE and/or MH term. This will be a minor problem for the reviewers and thus no comment needs to be sent to Moderna. See example below.

- 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

- In study p301, 25 subjects had AEs with an AEOUT= RECOVERED/RESOLVED or RECOVERED/RESOLVED WITH SEQUELAE, but an end date or collected duration is not provided. They need to clarify if AEOUT is correctly reported (in which case an end date should be provided) or if AEOUT is incorrectly reported. If incorrect they need to correct dataset accordingly.
- In study p301, 6 subjects had AEs with an AEOUT= NOT RECOVERED/NOT RESOLVED, but an end date is provided. They need to explain and correct where in error.
- Regarding ongoing solicited events:
  a. We previously had requested that reactogenicity events lasting beyond day 7 and collected in the Form: "Medical Attention Day" be mapped to FACE for the day-to-day information instead of FAAE. We will not request that they update the data in FACE with the data in FAAE for this submission; however, in any future submission it will need to be done as requested.
  b. We have found 2428 records in p301 in which reactogenicity events reported in CE and lasting longer than the 7-day evaluation period (CERFTDTC + 6) were not reported in the AE dataset, e.g., subject 300-2231 had myalgia from Day 3-16 as reported in CE, but myalgia was not reported in AE for this subject's ongoing event following dose 1. They need to update the AE dataset if these events should have been reported as ongoing.
  c. Ongoing was not flagged in CE as requested, instead they flagged an event in suppae with "Y" for "solicited adverse reaction" and "N" for "AR remove flag" which does not allow us to analyze the data very easily. They need to update the CE dataset by including "ongoing" in CEENRTPT with CEENTPT of "Day 7."
  d. We have found events in AE that were neither an ongoing solicited event nor an SAE, but which were categorized as "reactogenicity" in AECAT. We realize that they may have categorized events that were reported by the investigator which were synonymous with solicited events and which occurred during the 7-day evaluation period and which may have been merged into the CE dataset as such, but that causes a great deal of confusion when analyzing the data. The events should have been reported in CE from the start, but since they did not implement our requested way to report this data in the EUA submission in November 2020 we agreed that they could flag these events in suppae indicating they were "removed" from AE analysis and instead were included in the CE dataset and ultimately the reactogenicity analysis.
  e. We have found events that are reported in the Events datasets and Findings About datasets which are not linked together to provide a total picture for the event in analysis, e.g., subject 300-2215 had lymphadenopathy reported in CE (on Days 2-null), FACE (on Days 2 and 7), AE (on Days 7-9) and FAAE (2 rows provided for event but no days are indicated). In ADARSUM the number of days for underarm gland swelling or tenderness is 2 days which appears to be

incorrect. ADAE also has the event as Day 7-9. They need to correct all events in which this situation may have occurred.

- There are 456 records where reactogenicity events are reported in the AE dataset instead of the CE dataset. What appears to be the problem for many of these records is the term used in AE vs the terms used in CE, CE has "Underarm Gland Swelling or Tenderness" and in AE there are various terms that are equivalent to underarm gland swelling or tenderness.
- We have found several instances where events reported in AE were erroneously categorized as "Reactogenicity", e.g., subject 305-2061 had a left knee torn meniscus with AECAT= reactogenicity (see "reactogenicity in AE but not CE" report). They need to ensure that all events in AE are characterized correctly and resubmit the AE dataset. In addition, they need to know that none of the events correctly categorized as "reactogenicity" should be included in ADAE.
- We have found instances where CE was not updated with the investigator collected info, e.g., subject 301-2023 had severe underarm gland tenderness on Day 29 (Dose 1 day 1) in AE and in CE the event was reported as occurring Days 30-33 with moderate severity. In ADARSUM underarm gland tenderness number of days is 4 instead of 5 and the worst analysis toxicity grade is "repeated use…" They need to correct all datasets where this may have occurred.
- We have found 3290 records in p301 where ongoing reactogenicity events reported in the AE dataset have either the start date or the end date not equal to the dates reported in CE. This not only causes confusion on the actual dates/days of occurrence, but also becomes problematic in discerning which events are ongoing. For example, erythema was reported for subject 300-2107 in which the days of the event are 31-37 in CE and 31-36 in AE (dose 2). They need to ensure consistency of the dates/days reported for each reactogenicity event in CE and AE and correct where it is in error.
- They need to provide a rationale for reporting in the MH dataset a "New onset type 2 diabetes" for subject US326-2100 in P301 in which the subject was vaccinated on Aug 5, 2021 and the start date of the event was Mar 26, 2021; and "Depression" for subject US325-2195 in which the subject was vaccinated on Aug 15, 2020 and the start date of the event was Nov 3, 2020. They should report these events in the AE dataset if the dates are correct.
- We have found the start date or end date of an event missing in CE even though FACE and FAAE had each day reported, e.g., 301-2053 had underarm gland swelling on Day 2, 5, 6, and 7 in FACE and Day 9-15 in FAAE. This subject also had the event reported in AE from Days 6-16. ADARSUM has duration as 12 days. This event is also reported in ADAE (not only does it not belong in ADAE but it is also from the subject's diary per FAAE). Pain at injection site is also (double) reported to occur from D1-21 in ADAE and 20 days of pain in ADARSUM. They need to update the CE dataset with the dates/days.
- The duration of solicited adverse reactions appear to be calculated based on the number of unique days in which the event is reported not necessarily the total days that an event may have occurred. We are concerned that this underestimates the event duration (an event reported on Day 1 and Days 3 and 5 likely had lasted 5 days as opposed to 3).
- We previously had requested (April 2021) that if symptoms (recorded in the COVID diaries and reported in the FAEF dataset) were not due to a subject having COVID-19 (as determined to be

negative for COVID-19 and reported in MB), but were instead due to a solicited event occurring within the solicited assessment period for reactogenicity (7 days) for subjects in safety subset, be summarized in CE in conjunction with events reported in FACE and to also provide a flag that part or all of the data was from the COVID diary. We have found that this was not implemented in the datasets submitted to the BLA, for example, subject 300-2003 was determined to be COVID-19 negative on Day 1 and 3 (as reported in MB) yet the COVID-19 symptoms reported in CE under the CECAT "efficacy" including myalgia (mild on Day 3) and fatigue (mild on Day 3) were not included with the events under CECAT "reactogenicity" which were reported as myalgia (mild on Day 2) and fatigue (mild on Days 1-2). We requested that the CE dataset (and FACE if that is the dataset being used to report the ADARSUM dataset) be updated with this information. In addition, efficacy was not reported as we had requested, instead they did the following:

- All subjects with a "like" illness are reported in FAEF and CE (as requested).
- Instead of "COVID-19 confirmed" in CE, subjects with confirmed COVID-19 have row for "event meets the charter definition of COVID-19 and/or severe COVID-19 Diagnosis" n=1943 records
- They also may have a row where COVID-19 was not the diagnosis "Not a charter-defined Event" (i.e., does not meet the definition of any of the above) n=136 records. They have this as a term in CE but they don't use CEOCCUR to indicate Y or N which is not how events are to be reported in CE.
- In AE they have events "COVID-19" (n=1182 records) and "COVID-19 pneumonia" (n=17 records) in AEDECOD. Why does COVID-19 (n=1182) in AE not equal charter defined COVID-19 (n=1943) in CE? The terms are used too loosely.

Even so the CBER statistical reviewer should be able to explain how they derived the cases of COVID-19 from the results provided in SDTM (FAEF, CE, MB, AE, EX, DS).

- They 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." They will need to implement this in any future submission.
- 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. They need to correctly subcategorize these events. If the event does not need a subcategory then AESCAT can be null. Other subcategories that we are suggesting for AEs besides PIMMC are "NOCD" and "Exacerbation of a chronic disease."
- Medication provided to either prevent or treat solicited events should be reported in CM instead of or in addition to suppvs. They need to confirm that any future datasets will include this information in CM.

An IR was sent based on the comments above on September 24, 2021 to Moderna. It was separated into 3 groups based on priority and relatedness. We received a response from Moderna to the priority 1 group comments on October 8, 2021 (amendment 10), a response to the priority group 2 comment on October 14, 2021 (amendment 11) and a response to the priority group 3 comments on October 25, 2021 (amendment 14). The responses to priority group 1 were inadequate as they didn't revise the

datasets as requested, but rather indicated they would look into these issues and maybe fix them in the future. The response to priority group 2 was also inadequate. They indicate that they included all symptoms reported in the COVID diary in their efficacy analysis regardless if they were positive or negative for SARS-CoV-2. The responses to priority group 3 are adequate, however they indicate that they are unable to report in the CM domain, medication to either prevent or treat solicited events as more information would be required for records in CM domain.

For the inadequate response to the priority group 2 comment we sent another IR on October 22, 2021 requesting that a sensitivity analysis be performed for the rates of solicited adverse reactions by including all relevant events (occurring within the 7 days post vaccination) from the e-diary captured as COVID-19 symptoms that were negative for SARS-CoV-2; and to also perform a similar sensitivity analysis for unsolicited AEs for those events that occurred beyond 7 days of vaccination. A response was provided on October 29, 2021 (amendment 16). They did provide the sensitivity analysis; however, they requested further clarification on what is needed for it. Clarification was provided in the teleconference held on October 29, 2021. The sensitivity analysis will be reviewed by the statistical and clinical reviewer.

For the inadequate responses received to the priority group 1 comments we requested a teleconference with Moderna to reinforce what and why the datasets needed to be revised. Moderna was sent ten discussion items along with 2 corresponding reference spreadsheets (p301 reactogenicity missing from AE, and p301 reactogenicity in AE but not CE) on October 28, 2021 and was asked to comment on the impact each item had on the solicited and/or unsolicited safety results as well as update and resubmit the CBER Requested Tables. A teleconference was held on October 29, 2021. Moderna agreed to provide the information and update datasets as requested.

Moderna provided meeting minutes and responses to some of the comments on November 5, 2021 in amendment 18 to the teleconference held on October 29, 2021. In their response they had several questions which required input. A response to their questions as well as comments below concerning their CE mapping examples were sent to Moderna on November 19, 2021.

- Regarding 4a - Moderna proposed to re-submit the following domains with application of the updated lookup table: • CE, • FACE, • FAAE and • AE; and to re-submit the analysis of duration of SAR using CBER's definition of last day-first day+1. As the impact on other SAR analyses is minimum, the Sponsor proposed not to re-run other analyses of SAR. We agreed with this proposal.
- Regarding 4b – Moderna accepted CBER's comment and agreed to update CE domain adding CENRTPT= "Day 7" and CEENTPT= "ONGOING" for all events that last beyond Day 7. Moderna would like to propose to implement CBER's suggestion in the future sBLA submission. We responded that the ongoing flag should be reported in CE for any future sBLA and any future EUA submissions.
- Regarding 4c – Moderna provided a table in which suggestions are offered to flag events that are categorized as reactogenicity but may be in error or cause confusion. They suggested AESCAT=Missing Reported within 7 days for those events which are a reactogenicity event and

have a REMOVEFL=Y in suppae. We recommended that instead an AESCAT = included with subject diary data. The other subcategories suggested for ongoing reactogenicity events and for the wrong category were acceptable.

In the situation where there are both subject-reported event and investigator assessments contributing to CE topline records (example 2), regarding EVAL, at TC, CBER suggested to use "INVESTIGATOR". In order to keep traceability, Moderna proposed "STUDY SUBJECT/ INVESTIGATOR". We responded that although "Investigator" was sufficient we agreed with the proposal to use "Study Subject/Investigator".

Regarding 10 - During the teleconference we indicated that if the event began on Day 6, within the eDiary assessment period, it should be a SAR that is ongoing and subsequently analyzed in ADAR (not ADAE). Moderna provided CE-mapping examples to which the following comments were conveyed:

For Case 2: a. CESTDTC can be 2020-11-23.
b. CEENDTC – it is unclear if that is the end date as information was not provided on the event until resolution.
c. CEENRTPT and CEENTPT may not be null.

For Case 4: It is unclear if the CEENDTC, CEENRTPT and CEENTPT are correct as the event could be ongoing.

For Case 5: It appears that CESTDTC should be 2020-09-30

The updated datasets CE/SUPPCE, FACE/SUPPFACE, FAAE/SUPPFAAE and AE/SUPPAE were provided in amendment 27 on December 1, 2021. A summary of the updates implemented in the datasets include:

1. Solicited Symptom "lookup table" update: Dictionary-Derived Term (AEDECOD) map to prespecified symptoms (updated lookup table is included in this submission).

2. Added subcategory AESCAT if AECAT = "REACTOGENICITY"
   a. "SAE/Ongoing-Local or SAE/Ongoing-Systemic" – it is a clear flag although some of the events with this flag are not actually solicited, e.g., injection site induration, limb discomfort.
   b. "Included with Subject Diary Data" – it is a clear flag with all events having a remove flag in suppae
   c. "Wrong Category" - this includes solicited events and unsolicited AEs that were categorized as "reactogenicity". Only a few of the true solicited events in this subcategory are flagged with a remove flag in suppae. Even though this was not done it does appear that a majority of the events in AE with this subcategory have been incorporated or are already encompassed in the CE dataset and thus the FACE dataset. As the statistical reviewer is using the FACE for analysis, the event should be appropriately captured. There will still be some events where the duration in CE/FACE may not be accurate as the event from AE was not included as evidenced by the

example below. This will mean that some of the events will be analyzed as an unsolicited event in ADAE.

pls	Unique Subject Identifier of Subset of AE	Sequ enc...	Reported Term for ...	Dictionary-Derived Term	Category for Adverse Event	Subcateg ory for ...	Study Day ...	Study Day ...
2	mRNA-1273-P301-US300-2312	3	PHARYNGITIS	Pharyngitis	REACTOGENICITY	WRON...	99	113
3	mRNA-1273-P301-US303-2089	1	HEADACHE, ...	Headache	REACTOGENICITY	WRON...	29	52
4	mRNA-1273-P301-US304-2013	1	FATIGUE	Fatigue	REACTOGENICITY	WRON...	16	22

7/1 Cols	Unique Subject Identifier	Reported Term for the Clinical Event	Category for Clinical Event	Clinic al ...	Study Day ...	Study Day ...	Duration
591117	mRNA-1273-P301-US303-2089	Pain	REACTOGENICITY	Y	29	•	
591118	mRNA-1273-P301-US303-2089	Headache	REACTOGENICITY	Y	29	•	

3. CE Updates included:
   a. CE data source – they indicate that both a solicited event captured in e-DIARY and a solicited event captured in Adverse Event where AECAT = "REACTOGENICITY" and AESCAT = "WRONG CATEGORY" is included. This is mostly the case but not always, see discussion above.
   b. Adding CECAT = "IMMEDIATE REACTION" row for a solicited event occurring within 30 minutes after each dose
   c. Start date and end date were reported in CE in CESTDTC (earliest event date time (CETOXGR > 0) by Participator, Dose #, and Symptom) and CEENDTC (latest event date time (CETOXGR > 0) by Participator, Dose #, and Symptom).
   d. CEENRTPT = "ONGOING" and CEENTPT = "DAY 7" were added to the CE dataset if an event lasted beyond day 7. However, even with the addition of this flag new issues were identified.
      i. Ongoing records in CE=12592 (minus 5871 immediate events = 6721 and minus 66 day 6 (planned time point) events = 5937) and ongoing records in AE = 3915 have a total record count which do not match. In a follow-up question sent to Moderna on December 16, 2021 we asked for a rationale. On December 21, 2021, Moderna responded that the missing results in AE may be due to two possibilities:
         - 1892 of 6721 ongoing symptoms have no investigator assessment. They are reviewing each line item to record the discrepancy, so that it is not repeated in the future.
         - 970 of 6721 ongoing symptoms have investigator assessment, but event ending day is with day 7, this is a known issue and could be due to any of the following: eDiary (participant reported data) cannot be changed once submitted; eDiary and eCRF are two independent systems; investigator assessments does not agree with participate reporting data via eDiary.

      Their explanation does provide some clarity but a comment regarding future datasets will need to be sent to Moderna since the CE dataset is supposed to include investigator assessment. Regardless of their explanations and continued errors in CE, since the reviewers deemed the FACE and FAAE dataset to be the most accurate, the CE inaccuracies will not impact our final analysis.
   e. It appears that new data may be present in the revised CE dataset, e.g., subject US317-2261 had a new event in CE that began and ended on Day 8. This event was also reported in the FACE

dataset. In the initial CE dataset 149 events began on Day 8 and in the revised CE dataset 228 events began on Day 8. On December 16, 2021 we reiterated that if the event began after the assessment period it should be considered unsolicited and be reported in AE. If the event occurred on day 7 but was collected on Day 8 (which it appears many of these were) to include this with the summary of the event in CE. In the response on December 21, 2021, Moderna indicated that event days are separated by 24 hours from time of exposure. Thus the Calculated Event Start Day = [(Event Date Time (in Second) - Dose Date Time (in second)]/(3600*24) Set Start Day to 7 if the results are <7.5. This is valid but confusing. We need to ensure that days of the event are calculated similarly between all sponsors/applicants so that a reported Day 8 is not actually Day 7.

f. They do not need to flag ongoing for the immediate events or for any of the other days besides day 7 (in the future comment).

4. A total of 28 axillary lymphadenopathy (ipsilateral or bilateral) events beginning within the 7-day assessment period are still remaining in the revised AE dataset (AECAT= Adverse Event) in subjects that are in the solicited AE group. They may not all be reported in FAAE, e.g., subject 329-2284 had the event from Day 3-72 in AE, but nothing is reported in FAAE and in FACE the event is reported to occur from Day 36-41. This means the event would not be counted in the analysis of solicited lymphadenopathy. In our December 16, 2021, IR we asked Moderna to provide additional information on the steps taken in SDTM to remove these events from the ADAE analysis dataset and include them in the ADCE analysis dataset. In the response received on December 21, 2021, Moderna reiterated that the flag AESOFL= "N" indicates the event was not marked by the investigator as a solicited adverse reaction and thus would remain in AE. It is unclear why this was reiterated as this flag was previously discussed as being fraught with errors. They also reiterated that lymphadenopathy events starting on or after Day 8 would remain in AE which we had previously indicated was appropriate. Although they did not revise the AE dataset as requested, ultimately the 28 events will be included in the analysis of unsolicited adverse events and thus will be part of the safety information presented in the label.

Final conclusion:

Overall the datasets were adequate although not ideal for the statistical and clinical reviewer to use to verify the safety and efficacy results. Moderna does indicate that they have proactively taken actions to redesign the eCRF forms for future studies so that the reported data will be standardized according to our guidance and advice.

Data Fitness Findings Report

BLA125752

ModernaTX, Inc., September 2021

Findings	Notes
mRNA-1273-P301 **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*	

Document / Standard	Version	Notes
annotated CRF		Seems fine
SDTM Implementation Guide	SDTM-IG v3.2	
SDTM Controlled Terminology	2020-09-25	
SDTM define.xml	V2.0	Stylesheet has incorrect filename('define1-0-0.xsl'). It has to be changed to 'define2-0-0.xsl' to be able to view define.
Medications Dictionary	WHODD GLOBALB3Mar20	
Medical Events Dictionary (MedDRA)	V23.0	
SDTM Reviewer's Guide		Seems fine

From cSDRG: The data cutoff date (DCO) is defined as the date by which all data records in the clinical datasets will be included in or excluded from a prescribed set of analyses. For BLA submission, the DCO date is the date of data cutoff date (26-Mar-2021) with exceptions of data related to unblinding, death, serious adverse events (SAE), COVID-19 symptoms, and pregnancy. mRNA-1273-P301 Data Cutoff Algorithm.pdf is described in the details

Data Issues

Inconsistent coding of the exact same adverse event term

- 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

- cSDRG explanation: Confirmed with Coding Group, No Issue.

Inconsistent coding of the exact same medical history term

- 2 (distinct) MHTERMs

mhterm	mhllt	mhdecod	mhhlt	mhhlgt	mhbodsys	count_ of_mhs	med drav
BOTOX (FOREHEAD)	BOTULINUM TOXIN INJECTION	BOTULINUM TOXIN INJECTION	THERAPEUTIC PROCEDURES NEC	THERAPEUTIC PROCEDURES AND SUPPORTIVE CARE NEC	SURGICAL AND MEDICAL PROCEDURES	4	23
BOTOX (FOREHEAD)	DERMAL FILLER INJECTION	DERMAL FILLER INJECTION	SKIN AND SUBCUTANEOUS TISSUE THERAPEUTIC PROCEDURES NEC	SKIN AND SUBCUTANEOUS TISSUE THERAPEUTIC PROCEDURES	SURGICAL AND MEDICAL PROCEDURES	3	23
BOTOX INJECTIONS FOR COSMETIC PURPOSES	BOTULINUM TOXIN INJECTION	BOTULINUM TOXIN INJECTION	THERAPEUTIC PROCEDURES NEC	THERAPEUTIC PROCEDURES AND SUPPORTIVE CARE NEC	SURGICAL AND MEDICAL PROCEDURES	1	23
BOTOX INJECTIONS FOR COSMETIC PURPOSES	SKIN COSMETIC PROCEDURE	SKIN COSMETIC PROCEDURE	SKIN AND SUBCUTANEOUS TISSUE THERAPEUTIC PROCEDURES NEC	SKIN AND SUBCUTANEOUS TISSUE THERAPEUTIC PROCEDURES	SURGICAL AND MEDICAL PROCEDURES	1	23

- cSDRG explanation: Confirmed with Coding Group, No Issue.

AEOUT = NOT RECOVERED/NOT RESOLVED, but an end date is provided

- 6 records
- cSDRG explanation: Data collection issues due to ongoing status of the study
- For details, see report "BLA125752 - p301 - AEOUT vs AEENDTC.xlsx"

AEOUT = RECOVERED/RESOLVED or RECOVERED/RESOLVED WITH SEQUELAE, but an end date or collected duration is not provided

- 25 records
- Note that 8 of these records also have AEENRF = ONGOING
- cSDRG explanation: Data collection issues due to ongoing status of the study
- For details, see report "BLA125752 - p301 - AEOUT vs AEENDTC.xlsx"

There are adverse events marked DRUG WITHDRAWN, but the subject doesn't have a corresponding (ADVERSE EVENT) DS record

- 17 subjects
- See report "BLA125752 - p301 - AEACN is DRUG WITHDRAWN but no DS ADVERSE EVENT record.xlsx"

Reactogenicity events lasting longer than the evaluation period (CERFTDTC + 6), but not in AE dataset

- Joining on USUBJID and –LNKGRP (according to RELREC) results in 2428 records
  - See report for details: "BLA125752 – p301 - Reactogenicity missing from AE.xlsx"

Reactogenicity events in AE dataset but either start date or end date doesn't equal dates in CE

- 3290 records
  - See report for details: "BLA125752 – p301 - Reactogenicity date mismatch between CE and AE.xlsx"

Reactogenicity events in AE dataset but not in CE (using USUBJID and LNKGRP to join)

- 456 records
  - Note that all of these AEs have AESPID populated, but not AELNKGRP. And there is no matching value in CE (no CESPID, etc)
  - See report for details: "BLA125752 – p301 - Reactogenicity in AE but not CE.xlsx"

MHSTDTC is after RFSTDTC

USUBJID	MHTERM	MHDECOD	MHSTDTC	RFSTDTC
mRNA-1273-P301-US325-2195	DEPRESSION	Depression	2020-11-03	2020-08-15T11:56
mRNA-1273-P301-US326-2100	NEW ONSET TYPE 2 DIABETES	Type 2 diabetes mellitus	2021-03-26	2020-08-05T13:57

• cSDRG explanation: Data collection issues due to ongoing status of the study	

Application: BLA125752
Study: mrna-1273-p301
EDR Sequence: 0003

Generated: 2021-09-09T15:11:09
Version: 2.5.3
Data Standards Training
EDR Link: \\cber-fs3\m\eCTD_Submissions\BLA125752\0003\m5\datasets\mrna-1273-p301\tabulations\sdtm
EDR Link: \\cber-fs3\m\eCTD_Submissions\BLA125752\0003\m5\datasets\mrna-1273-p301\analysis\adam\datasets

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

Summary

Documents

SDTM Define.xml
Study Data Reviewer's Guide
ADaM Define.xml
Analysis Data Reviewer's Guide

Standards / Dictionaries

SDTM-IG 3.2
MedDRA 23.0

Subjects / Actual Arms

32102 - Subjects
1751 (5.5%) -
15185 (47.3%) - A
2517 (7.8%) - PLA
12649 (39.4%) - PLAA

Datasets

48 - Total SDTM Datasets
1 - Custom Datasets
18 - Suppqual Datasets
24 - ADaM Datasets (ADAE, ADAR1, ADAR2, ADARP7 ADARSUM, ADCM, ADDV, ADEFF, ADEFF2, ADEFF3, ADEX, ADIS, ADMB, ADMH, ADRISK, ADSL, ADSLSF, ADSYMP, ADTTE, ADTTEA, ADTTEB, ADTTRE, ADTTRE2, ADV

Reports to Help Basic Review Activities

Deaths
Death Summary
Death Details

Adverse Events
Adverse Events Coding Quality

Disposition
Disposition Coding Quality

Supplemental Info
Supplemental Contents

Potential Data Quality Findings

Demographics
1,291 of 32,102 (4.0%) RACE values not found in CDISC codelist
1,751 of 32,102 (5.5%) values for required variable ACTARM are missing
6 of 32,102 (< 0.1%) values for required variable SEX are missing
1,679 of 32,102 (5.2%) values for required variable ARMCD are missing
1,679 of 32,102 (5.2%) values for required variable ARM are missing
1,751 of 32,102 (5.5%) values for required variable ACTARMCD are missing
83 of 32,102 (0.3%) subjects have a different actual arm than planned
76 of 32,102 (0.2%) subjects are missing important dates in demographics

Disposition
6 of 165,978 (< 0.1%) disposition events are missing Start Date/Time of Disposition Event (DSSTDTC) and Study Day of Start of Disposition Event (DSSTDY)
17 of 165,978 (< 0.1%) disposition statuses or protocol milestones are potential duplicates

Exposure
27 of 84,320 (< 0.1%) values for required variable EXTRT are missing
181 of 84,320 (0.2%) treatments have ended after the last disposition date

Adverse Events
23 of 39,215 (< 0.1%) values for required variable AEDECOD are missing
23 of 39,215 (< 0.1%) values for required variable AETERM are missing
92 of 39,215 (0.2%) events are missing start time-point
3,048 of 39,123 (7.8%) adverse events have started after the last disposition date
11 of 39,192 (< 0.1%) adverse events are potential duplicates
39 of 39,215 (< 0.1%) adverse events have neither severity or toxicity grade populated

Clinical Events
138,742 of 763,643 (18.2%) events are missing start time-point
170,374 of 763,643 (22.3%) clinical events are potential duplicates

Laboratory
3 of 44,152 (< 0.1%) laboratory test results are potential duplicates
10,000 of 32,102 (31.2%) subjects are either missing a lab test or a baseline value

Vital Signs
2,339 of 2,155,392 (0.1%) vital sign results are potential duplicates

General Findings
Study data is missing important variables
Study events are missing end time-points
Study subjects are missing all baseline flags for all tests present in the dataset
Standard Results (--STRESC) or Standard Units (--STRESU) are missing

Traceability
1,679 of 32,102 (5.2%) subjects in SDTM DM are not included in ADSL
1,459 of 39,215 (3.7%) Adverse Events in SDTM AE are not present in ADAE
Treatment Emergent Flag in ADaM is inconsistent with Treatment Emergent Flag in SDTM