U.S. FOOD & DRUG ADMINISTRATION

# Information Request

Our Reference: STN: 125752/0

Information Request #2

Date: September 17, 2021

To: Michelle Olsen, Ph.D.
Moderna TX, Inc.
Email: Michelle.Olsen@modernatx.com

From: Josephine Resnick, Ph.D.
DVRPA/OVRR/CBER
Email: Josephine.Resnick@fda.hhs.gov

Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: Clinical: SMQs, severe COVID

Our review of your August 24, 2021 submission (STN 125752/0) is ongoing. We have the following requests for additional information:

Please respond to the following request by September 21, 2021:

1. Please submit an analysis of vaccine efficacy against severe COVID-19 cases using the CDC definition (hospitalization, admission to the ICU, intubation or mechanical ventilation, or death).

Please respond to the following requests by September 27, 2021:

2. With regards to the SMQ analyses (Tables 65-110 in CBER Requested Tables) submitted under Amendment 3 to the BLA, please submit the same SMQ analyses using Part B data.

3. Please provide the following additional SMQ analyses that are separate analyses for Part A and Part B (as separate documents). Please provide as separate tables SMQ analyses with broad and narrow terms combined and SMQ analyses with narrow terms only.
    a. Ischemic heart disease

b. Cardiac arrhythmia
c. Cardiac failure

4. The following comment is provided as a clarification and applies to all requested SMQ tables.

   For each SMQ, please provide a table for each study part (Part A, Part B as separate documents) with the relevant study groups in each (Part A: mRNA-1273, Placebo; Part B: mRNA-1273, Placebo, Placebo-mRNA1273). Please provide a separate table for broad (including narrow events) and narrow SMQ searches. For each table provide the following information:

   - # of events reported for each term for each group
   - 'n' participants and percentage (%) who reported each term for each group

   Example Table Shells:

Table xx: Participant Incidence of *SMQ Name*, Broad and Narrow Scope (Safety Set) - Part A

| Preferred Term | mRNA-1273 (N= ) | | Placebo (N= ) | |
|---|---|---|---|---|
| | # of Events | n (%) | # of Events | n (%) |
| Any *SMQ Name* terms | | | | |
| PT 1 | | | | |
| PT 2 | | | | |
| ... | | | | |
| PT n | | | | |

Table xx: Participant Incidence of *SMQ Name*, Narrow Scope (Safety Set) - Part A

| Preferred Term | mRNA-1273 (N= ) | | Placebo (N= ) | |
|---|---|---|---|---|
| | # of Events | n (%) | # of Events | n (%) |
| Any *SMQ Name* terms | | | | |
| PT 1 | | | | |
| PT 2 | | | | |
| ... | | | | |
| PT n | | | | |

Table xx: Participant Incidence of *SMQ Name*, Broad and Narrow Scope (Safety Set) - Part B

| Preferred Term | mRNA-1273 (N= ) | | Placebo (N= ) | | Placebo-mRNA-1273 (N= ) | |
|---|---|---|---|---|---|---|
| | # of Events | n (%) | # of Events | n (%) | # of Events | n (%) |
| Any *SMQ Name* terms | | | | | | |
| PT 1 | | | | | | |
| PT 2 | | | | | | |
| ... | | | | | | |
| PT n | | | | | | |

Table xx: Participant Incidence of *SMQ Name*, Narrow Scope (Safety Set) - Part B

| Preferred Term | mRNA-1273 (N= ) | | Placebo (N= ) | | Placebo-mRNA-1273 (N= ) | |
|---|---|---|---|---|---|---|
| | # of Events | n (%) | # of Events | n (%) | # of Events | n (%) |
| Any *SMQ Name* terms | | | | | | |
| PT 1 | | | | | | |
| PT 2 | | | | | | |
| ... | | | | | | |
| PT n | | | | | | |

5. In the ADAE dataset, there are at least 378 records that have an AESTDTC value with a time code of "T00:00" and ASTDTM values with time codes of '12:00:00 AM'. It is likely that these times are derived due to a lack of a time input. The 49 of these records that occur on study day 1 are all found to be not treatment emergent (TRTEMFL = ""), however that is unclear because of the derived time issue. Can you please provide additional clarification on these 49 records and if they occurred after the first dose of treatment on study day 1.

Please respond to the following request by October 4, 2021:

6. For the PTs in which there is an observed imbalance (mRNA-1273 or placebo-mRNA-1273 > placebo), please provide in Excel sheet format a summary of demographics and relation to last vaccination for the subjects who contributed to the PT.

| Treatment | Subject | Age / Sex / Race | Adverse event | Relative Day to Last Vaccination and Dose # |
|---|---|---|---|---|
| mRNA-1273 | 123456 | 56 / F / WHITE | Tachycardia | 2 (dose 2) |
| mRNA-1273 | 78910 | 77/M/Asian | Tachyarrhythmia | 14 (dose 1) |

Please confirm your receipt of this request, and provide your responses as amendments to STN 125742/0 at your earliest convenience but no later than the dates specified for each item above.

Please contact me if you have questions and include Sudhakar Agnihothram (Sudhakar.Agnihothram@fda.hhs.gov) and Joseph Kulinski (joseph.kulinski@fda.hhs.gov) on all communications.