U.S. FOOD & DRUG ADMINISTRATION

# Information Request

**Our Reference: STN: 125752/2**

**Information Request #15**

**Date:** November 3, 2021

**To:** **Michelle Olsen, Ph.D.**
ModernaTX, 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

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

1. On review your analysis for VE against asymptomatic infection, we have identified cases classified as asymptomatic infection where the participant was asymptomatic before and during the date of their positive RT-PCR or N-serology but then later went on to develop COVID-19 symptoms days/weeks after. Please conduct a sensitivity analysis for your endpoint of VE against asymptomatic infection excluding all participants who had any documented CDC or protocol-defined COVID-19 symptoms at any time during the entire study through the blinded phase of the study (including symptoms reported both before and after the positive PCR or N-serology result and symptoms reported during both the blinded phase and open-label phase of study).

2. For each efficacy endpoint presented in Table 6 of the Clinical Overview, please clarify the variables in ADSL used to define the time period considered in the analyses.

3. Please complete the following table for subjects who had suspected COVID-19 (met criteria for illness visit and nasopharyngeal swab collection) starting 14 days after Dose 2, but for whom no PCR results are not available:

| | mRNA-1273 | Placebo |
|---|---|---|
| Participants with suspected COVID-19 but no PCR result available | | |
| Reason for no PCR results | | |
| Not collected | | |
| Sample lost | | |
| Sample collected out of window | | |
| Other (please list) | | |

Please provide narratives for participants who would have met severe COVID-19 criteria, but who did not have PCR results available.

4. Regarding your data on variants and Genotyping Report (Appendix 16.5):

   a. On page 6 of your Genotyping Report, you indicate of the total adjudicated COVID-19 cases starting 14 days after Dose 2 in the PPS with sequencing data, there were 2 cases attributable to B1.117 variant in the placebo group compared to none in the mRNA-1273 group. However, B1.117 (or B.1.1.7) is not listed in any of the tables (Table 14.2.1.1.2.1.4.1 or 14.2.1.1.2.1.4.2). Please clarify this discrepancy and provide updated tables if applicable.

   b. Please provide summary table similar to Table 14.2.1.1.2.1.4.1 for number of variants by lineage when only including adjudicated cases **starting after 14 days after Dose 2** in the PP set.

   c. Please provide summary table similar to Table 14.2.1.1.2.1.4.1 for sequencing data from all available SARS-CoV-2 RT-PCR positive NP samples collected from July 2020 through May 2021 from participants in the blinded portion of the study, **regardless of symptoms**.

   d. For Table 14.2.1.1.2.1.4.1, in the number of events by lineage, only 17 events are listed out of the 56 mRNA-1273 participants with COVID-19 and only 545 events are listed out of the 769 placebo participants. Please update the table to classify the remaining events so that all 56 cases in mRNA-1273 participants and all 769 cases in placebo participants are accounted for (e.g., other variant—if this would be different than your

"none" classification, no sequencing data available, inconclusive sequencing data).

Please confirm your receipt of this request, and provide your responses as an amendment to STN 125752 at your earliest convenience but no later than November 8, 2021.

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.