Information Request

Our Reference: STN: 125752/2

Information Request #24

Date: November 29, 2021

To: **Michelle Olsen, Ph.D.**
ModernaTX, Inc.
Email: Michelle.Olsen@modernatx.com

From: **Joseph Kulinski, Ph.D.**
DVRPA/OVRR/CBER
Email: Joseph.Kulinski@fda.hhs.gov

Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: Asymptomatic infection, blinded efficacy follow-up

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

1. In your response to the November 12, 2021 clinical information request, you present in Table 1-3 examples of subjects that were incorrectly censored as a result of mis-labeled VISIT in IS and MB, resulting in inappropriate exclusion of cases, inclusion of non-cases, and cases with incorrect event dates for SARS-CoV-2 and asymptomatic infection. Please submit corrected analyses of efficacy against SARS-CoV-2 infection and asymptomatic infection starting 14 days after Dose 2 in the Per-Protocol Set during blinded follow-up. Similarly, please provide the corrected sensitivity analysis for asymptomatic infection from Item 1 of your response to the November 3, 2021 information request, copied below for your reference:

   From November 3, 2021 Information Request:
   On review of 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. Please fill in the following table for blinded follow-up for efficacy (from Dose 2 to PDV/unblinding) in the per protocol set:

Table 1. Blinded Follow-up Duration After Dose 2, Per Protocol Set

	mRNA-1273 (N=14287)	**Placebo (N=14164)**	**Total (N=28451)**
Median blinded follow-up post dose 2, days			
All participants			
≥18 to <65 years			
≥65 years			
Between 2 to <4 months blinded follow-up post dose 2, n (%)			
At least 4 months blinded follow-up post dose 2, n (%)			
Between 4 to <6 months blinded follow-up post dose 2, n (%)			
At least 6 months blinded follow-up post dose 2, n (%)			

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 December 2, 2021.

Please contact me if you have questions and include Sudhakar Agnihothram (sudhakar.agnihothram@fda.hhs.gov) and Josephine Resnick (josephine.resnick@fda.hhs.gov) on all communications.