U.S. FOOD & DRUG ADMINISTRATION

Information Request

Our Reference: STN: 125752/2

Information Request #9

Date: October 14, 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: CMC: TOR and CPD limits

Our review of your August 24, 2021 submission (STN 125752/2) is ongoing.

1. We have reviewed the information submitted in BLA Amendment 125752.1 regarding revision of the time out of refrigeration (TOR) and cumulative process duration (CPD) limits. We find that the proposed increase of the cumulative process TOR (15 – 25°C) from (b) (4) and cumulative process duration (2 to 8°C) and TOR (15˚C to 25˚C) from (b) (4) (b) (4) has not been adequately supported by quality data that you provided in section 3.2.P.2 Manufacturing Process Development {Comparability} and, therefore, is not acceptable.

   Please note that the proposed cumulative TOR and cumulative process duration upper limits (e.g., cumulative TORs of about (b) (4) and cumulative process durations of about (b) (4) may impact overall product consistency over the life-cycle of the product and increase the risk of releasing vaccine with RNA purity and impurity levels which are not representative of those of the clinical lots used to demonstrate effectiveness. Any changes in the specification for the cumulative TOR and/or the cumulative process duration should be supported with data from at least three lots manufactured at the most extreme time requested.

Until supportive data are available, the manufacturing process should be controlled such that the proposed limits for cumulative TOR and cumulative process duration are within the PARs used for the initial Scale B PPQ and the Phase 3 clinical lots to ensure consistent DP purity levels for registered commercial lots.

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 30, 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.