U.S. FOOD & DRUG ADMINISTRATION

Information Request

Our Reference: STN: 125752/1

Information Request #29

Date: December 9, 2021

To: **Michelle Olsen, Ph.D.**
ModernaTX, Inc.
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From: **Josephine Resnick, Ph.D.**
DVRPA/OVRR/CBER
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Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: Justification of Specifications

Our review of your August 16, 2021 submission (STN 125752/1) is ongoing. We have the following comments and requests for additional information:

To support the DP release and stability acceptance limits, please include the following information in section 3.2.P.5.6 *Justification of Specifications*:

1. In several IND communications including the CBER pre-BLA written responses from July 7, 2021, we had requested that a quantitative (b) (4) test be performed for DP release and stability monitoring. In the absence of such a (b) (4) test, please provide available quantitative (b) (4) (b) (4) results performed on DS or DP lots as a characterization test using your qualified (b) (4) or any other quantitative or semi-quantitative test. Please provide (b) (4) (b) (4) results for all DS or DP lots for which quantitative (b) (4) data are available at release or as part of stability studies together with data for RNA content (by AEX-HPLC), and RNA purity and product-related impurities (by RPIP-HPLC) from corresponding lots and time points.

2. Please include a description of the (b) (4) method (or any other quantitative characterization test method used) and a summary of results for the DS in section 3.2.S.2.6 *Manufacturing Process Development {Comparability Scale A to*

Scale B} and/or the DP in section 3.2.P.2 *Pharmaceutical Development {Comparability},* as applicable.

3. Please provide a justification for not performing a quantitative (b) (4) test as a quality release and stability test in section 3.2.P.5.6 *Justification of Specifications*.

4. Regarding the release and stability acceptance limit justifications and supportive data for RNA content (release and end of shelf-life: (b) (4) and RNA purity (release: (b) (4) and end of shelf-life: (b) (4) (b) (4) we acknowledge the analytical data provided for (b) (4) DP lots. In addition, please include:
    a. The clinical data from dose-ranging studies and effective delivery dose (EDD) ranges in Phase 3 studies, which support the proposed lower and upper limits for RNA content and lower limit for RNA purity.
    b. The data and statistical analyses used to derive the (b) (4) end of shelf-life limit for RNA purity.

5. Please provide information on the calculations used to estimate RNA purity release limits based on DP degradation curves, estimated degradation during storage and handling, and known assay variability. In addition, please provide report DPAD-00881 *Justification of Specifications for mRNA-1273 Purity Minimum Release Limit* submitted to EUA 27073 and updated degradation curve data for DP lots stored at the intended storage conditions.

Please confirm your receipt of this request and submit your response as an amendment to STN 25752 as soon as possible but no later than December 23, 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.