U.S. FOOD & DRUG ADMINISTRATION

Information Request

Our Reference: STN: 125752/2

Information Request #35

Date: December 16, 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: Validation of the (b) (4) method (SOP-1142)

Our review of your August 24, 2021 submission (STN 125752/2) is ongoing. We have reviewed your November 30, 2021 response to IR#18 (dated November 10, 2021), regarding validation of the (b) (4) method (SOP-1142). We do not agree with your responses for the validation parameters listed below. Please respond by the requested date above. If clarification is needed, please request a technical call as soon as possible.

1. In comment 6, we requested data to demonstrate linearity of (b) (4) (b) (4) The developmental data you provided using stability samples (b) (4), suggests linearity can indeed be demonstrated, however, the results cannot be accepted because the results were not from a study with predefined acceptance criteria. Please provide data from a protocol-driven validation study using samples generated by spiking DS/DP with stressed samples. Spiking should span the appropriate range (b) (4) for (b) (4) (b) (4) Please note, we do not agree with using the (b) (4) as a surrogate for (b) (4) Please evaluate linearity of (b) (4) independently, using (b) (4) in place of (b) (4) (b) (4)
2. In comment 7, we requested data to demonstrate the accuracy of measurements for (b) (4) As for the linearity data, we do not agree with using (b) (4) as a "surrogate" for (b) (4) (b) (4) since the assay has (b) (4)

(b) (4) In addition, the format in which you presented accuracy data is not correct: since the reportable result of the assay is (b) (4), accuracy should be determined as the (b) (4) Data should be provided for (b) (4) throughout the assay range (b) (4) (b) (4)

3. In comment 8, regarding intermediate precision (IP), your response stated that Table 4 in the validation report (QC-MVR-0025) provides the requested IP data, however, the data are system suitability results, not precision. The data in Table 7 and 8 include an assessment of repeatability for Analyst 1 and 2 at Norwood and Dedham, but data were not provided to demonstrate IP (i.e., assays performed on a different day/by different analyst at the same site) for each site. Please submit data to demonstrate inter-assay precision (IP) at each site.

4. In comment 9, your response stated the range (b) (4) of the method is (b) (4) for (b) (4) without providing data to support your claim. Range is demonstrated from linearity, accuracy, and precision and therefore data demonstrating acceptance criteria for each of these parameters are met should be provided at the lowest and highest (b) (4) in the range. The range should encompass the specification. Once you have established assay linearity, accuracy and precision for measuring (b) (4) (b) (4) independently, please determine the range of the method.

5. In response to comment 10 you provided Quantitation and Detection Limits (QL and DL) for (b) (4). Since (b) (4) have very different attributes, the (b) (4) cannot be used as a surrogate for the determination of their QLs and DLs. Please evaluate DL/QL experimentally and/or empirically for (b) (4) independently. Empirical QL can be determined from the linearity plot (b) (4) using the slope and standard deviation values of the regression line. Please provide the QL and DL, in (b) (4), for (b) (4) (b) (4)

Please confirm your receipt of this request and submit your response as an amendment to STN 125752 as soon as possible but no later than December 29, 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.