**Information Request**

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

**Information Request #8**

**Date:** October 6, 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: Analytical method procedure and validation

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

We have the following request for additional information regarding sample availability for in-support testing:

Drug Substance (DS)
Please provide 10 aliquots (100 µL aliquots preferred) of DS from three different lots and the following documentation and reagents in sufficient quantity to perform 10 independent tests for the following DS assays:

1. 5' – Cap assay
   a. (b) (4) (with COA)
   b. mRNA reference material (with COA)
   c. Cap guide
   d. Upper limit of backpressure of HPLC system during sample run
   e. Test result for each DS lot
   f. Please confirm that (b) (4) is used as the (b) (4) in sections 8.3.7.2 and 8.3.8.1 of SOP-0997.

2. % Poly A tail RNA
   a. mRNA reference material (with COA)
   b. Test result for each lot

Drug Product (DP)

Please provide 150 vials of DP per lot from three different DP lots and the following reagents and documentation for the following DP release assays:

1. Identity
    a. Positive Control: (b) (4) (Lot# (b) (4) )
    b. Positive control primers for (b) (4) sequencing
        (b) (4)
        (b) (4)
        (b) (4)
    c. Primers used for (b) (4) sequencing
        (b) (4)
        (b) (4)
        (b) (4)
        (b) (4)
    d. COAs with concentration/dilutions for use along with temperature of storage and expiry date

2. Total RNA Content
    a. mRNA reference material (with COA)
    b. Test result for each DP lot

3. Purity/Product-Related Impurities
    a. RNA reference material
    b. Test result for each DP lot

4. % RNA Encapsulation
    a. current mRNA-1273 LNP DP Positive control (working reference material)
    b. Formulation Buffer (20mM Tris,(b) (4) Sucrose, pH (b) (4) buffer), (b) (4) (b) (4)
    c. COAs with concentration/dilutions for use along with temperature of storage and expiry date

5. Particle Size
    a. Test result for each DP lot

6. Polydispersity
    a. Test result for each DP lot

7. Lipid Identification
    a. Standards for the 4 different lipids
    b. Test result for each DP lot

8. Lipid Content (mg/mL)
    a. Test result for each DP lot

9. pH
    a. Test result for each DP lot

10. In Vitro Translation
    a. Current Positive controls, CX-024414 or mRNA-1273 (b) (4)
    b. COAs with concentration/dilutions for use along with temperature of storage and expiry date

11. Bacterial Endotoxins
    a. Test result for each DP lot

Documentation
1. Please provide Certificates of Analysis for all reagents
2. Please provide results of the assays listed for the DS lots and DP lots submitted to CBER

The samples and reagents should be shipped to:
(Most) Nahid Parvin
Food and Drug Administration
Center for Biologics Evaluation and Research
Division of Biological Standards and Quality Control
10903 New Hampshire Avenue
WO75, G-640
Silver Spring, MD 20993

Please contact Marie Anderson at 240-402-6292 (marie.anderson@fda.hhs.gov) for questions regarding this request and to provide shipment date(s) and tracking number(s).

We request that these samples, reagents, and documentation be sent by October 25, 2021 or notify CBER by then when the shipment(s) can be expected.