U.S. FOOD & DRUG ADMINISTRATION

Information Request

Our Reference: STN: 125752/2

Information Request #13

Date: November 1, 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: CMC/Manufacturing

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

Please refer to the drug product (DP) cumulative process durations (CPD, listed in the Table below) applicable to the Catalent and Baxter DP manufacturing sites, which you indicated were qualified based on:

- Analysis of data from manufacturing experience at Catalent and Monte Carlo simulations which predict that DP release criteria for purity (b) (4)) will meet specification for(b) (4) of DP lots [Section 3.2.P.2.3.1.2.3 *Pharmaceutical development {Process Characterization}*].
- Hold-time qualification studies conducted as part of process performance qualification (PPQ) batches [Section 3.2.P.3.5.1.3.5 *Process Validation and/or Evaluation {Catalent}* and PPQ report VPPQ-256-100-00003-S for DP manufacture at Catalent].

Table – DP cumulative process durations

Process Parameter	PAR	Criticality Designation
Total cumulative process duration (refrigerate 2 to 8°C, TOR 20 to 25°C)	(b) (4)	Critical Process Parameter
Cumulative time out of refrigeration	(b) (4)	Critical Process Parameter

(TOR 20 to 25°C)		

Abbreviations: PAR = proven acceptable range; TOR = time out of refrigeration

We have the following comments:

1. Regarding report VPPQ-256-100-00003-S,
(b) (4)

2. Regarding the hold studies to support the process durations, you indicated that the CPD at CRT (TOR 15 to 25˚C) and total CPD were challenged during PPQ to establish the routine manufacturing hold limits with results presented for (b) (4) DP lots ((b) (4)) in section 3.2.P.3.5.1.3.5 *Hold Time Qualification,* Tables 26 and 27, and in the above cited PPQ report. We have the following comments regarding the validation study:

(b) (4)

3. In addition to qualification data (as detailed in item 1.c), you may support the CPDs with data from manufacturing experience. If you choose to use data from manufactured lots, please include results for all DP manufactured at Catalent and Baxter, including lots that did not meet release specifications. Please include CPDs at refrigerated 2 to 8°C, CRT (TOR 15 to 25˚C), and total (2 to 8°C, TOR 15 to 25˚C) and results for mRNA purity at release and any other parameters that were measured and may be affected by process duration. Please also specify the manufacturing step at which sampling for DP release testing occurred.

The following comment pertains to the DP stability program:

4. With regard to the DP stability studies and the DP shelf-life (i.e., expiry) please include the following information in stability sections 3.2.P.8.1 *Stability Summary and Conclusion* and 3.2.P.8.2 *Post-approval Stability Protocol and Stability Commitment* as appropriate,
    a. Please describe how the sampling was performed for DP stability studies for clinical lots and PPQ lots; specifically, the DP manufacturing step when samples were taken.

b. Please describe how the sampling will be performed for post-approval commercial DP release and stability studies at Catalent and Baxter. If samples are taken during filling, please specify the points during the filling step when samples are taken and the number of samples tested. If samples are taken after labeling or packaging, please specify the labeling or packaging step when samples are taken and provide the number of samples tested.

c. In section 3.2.P.8.1, please include and introductory section stating the shelf-life for the commercial DP when stored at the intended conditions and specify the manufacturing step considered the DP date of manufacture.

The following comment pertains to the DP release testing:

5. In DP section 3.2.P.5.1 *Specification(s*), please describe the release tests performed on the unlabeled vs. the labeled filled vials. In addition, please include the identity test performed as per 21 CFR 610.14 after all labeling operations are completed (i.e., vial and package labels).

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 12, 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.