U.S. FOOD & DRUG ADMINISTRATION

Information Request

Our Reference: STN: 125752/2

Information Request #28

Date: December 7, 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: Lot Release Protocol Template:

Our review of your August 24, 2021 submission (STN 125752/1) is ongoing. We have the following request for additional information regarding your Lot Release Protocol Template:

Note: Page numbers referenced below are from Adobe page numbering of your LRP template document QC-OTH-0609 submitted in STN 125752/1.

Throughout the document:

1. Footer
   - Please resolve the page numbering (current template has two different page numberings).
   - Please correct the overwrites.

2. Please review and ensure the test methods (including SOP) and acceptance criteria are correct. For example, on pages 4 and 9 of 12, please correct the test method SOP for purity and product-related impurities to SOP-1142. The LRP template currently references SOP-0996.

Page 1 of 12:

3. Please refer to page 4 of this document, for an example of the first page of an LRP template. Use this as the basis for page 1 of the Spikevax LRP template.

4. Please move the mRNA 1273 Drug Product Composition table to the page after the current page 3 of 12.

In addition, please note that in the header of the LRP, the reason for submission is checked as "Surveillance," which is incorrect. The LRP is intended for lots to be submitted for official lot release in accordance with 21 CFR 610.2 so please change this to "Release" for all lots submitted.

Pages 2 through 12 of 12:
5. Please remove the header. This information is should be on on page 1 only.

Pages 4 through 8 of 12:
6. Please remove the following tables:

- Table 1. (b) (4) and Production of DNA Plasmid - page 4
- Table 3. Manufacture of (b) (4) - pages 5 – 6
- Table 4. Manufacture of mRNA-1273 Lipid Nanoparticles, Drug Substance (DS) – pages 7 - 8

Please note that CBER expects the tests on the DNA Plasmid, (b) (4) (b) (4), and mRNA-1273 Lipid Nanoparticles Drug Substance to be performed and documented in accordance with 21 CFR 610.1, but we are requesting that only the results of testing of the CX-024414 mRNA and mRNA-1273 Drug Product be submitted to CBER for lot release.

Page 9 of 12:
7. For the In vitro translation test, please include additional information as stated in the proposed template below:

Test Samples	**Acceptance Criteria**	**Date of Test**	**Results**
Positive Control Lot#	(b) (4)		
DP sample			

Page 11 of 12:
8. Sterility test – please include the test method and test result details. Include the information as stated in the proposed template below:

SOP number: _____

On Test Date	Medium/Temperature	Number of vials tested	Off Test Date

Result:
Specification:

Sent Firm's Response from BLA. They are OK with releasing BLUE boxed information.

9. Endotoxin test – please include the test details. Include the information as stated on the proposed template below.

Limulus Amebocyte Lysate Test

Method ☐ (b) (4) ☐ (b) (4)

Test date _____

Name of Lysate Manufacturer _____

Lysate Lot number _____

Standard Curve Information

Endotoxin lot number _____

Endotoxin Mfr/Supplier_____

Standard Curve

	Standard Endotoxin Concentration IU/mL	Mean Onset Time (seconds)	CV%
1			
2			
3			
4			
5			
6			

Correlation coefficient (r): _____ Intercept: _____ Slope: _____

Product Test Summary

MVD _____

	Results IU/mL	Test Dilution	Mean Onset Time	CV%	% Spike Recovery
Beginning					
Middle					
End					

Results (IU/mL): _____ Specifications: _____

Calculations or additional comments

Appendix: Lot Release Protocol Template Page 1 example

cc: 000000 _0/Lic #/C or –B or –FC Page 1 of y
Lot Number:
License Name of Product:

Reason For Submission
__ For Release
__ For Surveillance
__ For Licensing Action
__ Corrected Protocol

Manufacturer Name:

STN:

Manufacturer Address:

Trade name:

Date of Manufacturing: 00/00/0000 Expiration Date: 00/00/0000

Label Strength: 00%

Source Material:

Processing Method:

Stabilizer: _____
Manufacturer / Lot Number

Other:

Reprocessing/Heating:

Fill Information

Filling Date: 00/00/0000

Location:

Total Volume: 000 mL Volume per Vial: 000 mL

Number of Vials filled: 0000 Number of Rejected Vials: 0000

Recommended Reconstitution Volume:

Storage Temperature:

All tests conducted on this lot are reported and pass specifications as required.

Signature: Date:

Printed name: _____ Title: Authorized Official

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 20, 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.