

**IND Number 19745**  
**Sequence No. 0081**

November 30, 2020

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Document Control Center  
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**Submission Type: Information Amendment – Chemistry, Manufacturing and Control  
Other – Response to Information Request**

Dear Dr. Gruber:

Reference is made to Investigational New Drug Application (IND# 19745) for mRNA-1273, a messenger RNA (mRNA)-based active immunization to induce protective immunity against acute respiratory disease associated with the SARS-COV-2 virus (Sequence No. 0001, April 27, 2020).

The purpose of this submission is to introduce Lonza as a site for (b) (4) and mRNA-1273 LNP manufacturing as well as to provide batch analysis, manufacturing process information, process validation/evaluation information, and an updated comparability assessment for the (b) (4) CX-024414 mRNA process initial PPQ lot manufactured at Moderna, the (b) (4) CX-024414 mRNA process GMP lot manufactured at Lonza (Portsmouth, NH), the (b) (4) process initial PPQ lot manufactured at Moderna, the (b) (4) process GMP lot manufactured at Lonza, the (b) (4) Final Scale B mRNA-1273 LNP process initial PPQ lot manufactured at Moderna, and the (b) (4) Final Scale B mRNA-1273 LNP process GMP lot manufactured at Lonza. In addition, updated reference standard information and minor revisions to drug product specifications have also been provided.

The revised Module 3 CTD sections, as described in the following table, are being submitted:

CTD Section		Changes
3.2.S.2.1 {CX-024414}	Manufacturer(s)	<ul style="list-style-type: none"> <li>Addition of (b) (4) (Final Scale B) production at Lonza Biologics, Inc.</li> </ul>
3.2.S.2.2 {CX-024414}	Description of Manufacturing Process and Process Controls	<ul style="list-style-type: none"> <li>Addition of (b) (4) (Lonza Biologics, Inc.) CX-024414 mRNA item number</li> <li>Revision to reflect ability to perform (b) (4) step to adjust RNA concentration</li> <li>Addition of (b) (4) (Lonza Biologics, Inc.) for (b) (4) Clarification, Post -Clarification Hold and Storage step</li> <li>Addition of post-filtration weight step and mixing during capping step</li> </ul>

3.2.S.2.3 {CX-024414}	Control of Materials {CX-024414-Starting Materials}	<ul style="list-style-type: none"> <li>• (b) (4)</li> <li>•</li> </ul>
3.2.S.2.4 {CX-024414}	Control of Critical Steps and Intermediates	<ul style="list-style-type: none"> <li>• Addition of Lonza specific microbial control for filter integrity testing.</li> </ul>
3.2.S.2.5 {CX-024414}	Process Validation and/or Evaluation	<ul style="list-style-type: none"> <li>• Removal of (b) (4) of CX-024414 manufacturing process at Lonza Biologics, Inc.</li> </ul>
3.2.S.2.5 {CX-024414 - Lonza}	Process Validation and/or Evaluation	<ul style="list-style-type: none"> <li>• Process validation information for (b) (4)</li> <li>• Inclusion of (b) (4) of CX-024414 Process Performance Qualification (PPQ) protocol (Lonza Biologics, Inc.)</li> </ul>
3.2.S.2.6 {CX-024414}	Manufacturing Process Development	<ul style="list-style-type: none"> <li>• Addition of information for (b) (4) Moderna PPQ lot comparability data</li> <li>• Addition of information for (b) (4) Lonza GMP comparability</li> </ul>
3.2.S.4.4 {CX-024414}	Batch Analysis	<ul style="list-style-type: none"> <li>• Addition of Lot 400742003 PPQ batch data</li> <li>• Addition of Lot 4007420010 (Lonza lot 943122) GMP batch data</li> </ul>
3.2.S.5 {CX-024414}	Reference Standard	<ul style="list-style-type: none"> <li>• Revised to include additional information for CX-024414 Reference Material program</li> </ul>

(b) (4)

(b) (4)

3.2.S.2.1 {mRNA-1273 LNP}	Manufacturer(s)	<ul style="list-style-type: none"> <li>Addition of (b) (4) Final Scale B Production at Lonza Biologics, Inc.</li> </ul>
3.2.S.2.2 {mRNA-1273 LNP}	Description of Manufacturing Process and Process Controls	<ul style="list-style-type: none"> <li>Addition of (b) (4) (Lonza Biologics, Inc.) mRNA-1273 LNP item number</li> </ul>
3.2.S.2.4 {mRNA-1273 LNP}	Control of Critical Steps and Intermediates	<ul style="list-style-type: none"> <li>Revision of microbial control information</li> </ul>
3.2.S.2.5 {mRNA-1273 LNP- Lonza}	Process Validation and/or Evaluation	<ul style="list-style-type: none"> <li>Inclusion of (b) (4) of mRNA-1273 LNP Process Performance Qualification (PPQ) protocol (Lonza Biologics, Inc.)</li> </ul>
3.2.S.2.6 {mRNA-1273 LNP}	Manufacturing Process Development	<ul style="list-style-type: none"> <li>Addition of information for (b) (4) Moderna PPQ lot comparability data</li> <li>Addition of information for (b) (4) Lonza GMP comparability</li> </ul>
3.2.S.4.4 {mRNA-1273 LNP}	Batch Analyses	<ul style="list-style-type: none"> <li>Addition of Lot 5007520002 PPQ batch data</li> <li>Addition of Lot 5007520009 (Lonza Lot 948548) GMP batch data</li> </ul>
3.2.P.2.4	Container Closure System	<ul style="list-style-type: none"> <li>Addition of studies to support use of multi-dose vial</li> </ul>
3.2.P.2.5	Microbiological Attributes	<ul style="list-style-type: none"> <li>Addition of studies to support use of multi-dose vial</li> </ul>
3.2.P.3.5	Process Validation and/or Evaluation	<ul style="list-style-type: none"> <li>Addition of information to support shipping validation</li> </ul>
3.2.P.5.1	Specifications	<ul style="list-style-type: none"> <li>Revision of particle size specification from (b) (4)</li> </ul>
3.2.P.5.6	Justification of Specifications	<ul style="list-style-type: none"> <li>Justification of revision of particle size specification</li> </ul>
3.2.A.1 {ModernaTX, Inc -Norwood}	Facilities and equipment	<ul style="list-style-type: none"> <li>Addition of room numbers associated with mRNA-1273 manufacturing</li> <li>Addition of reference to validation documents for utilities, HVAC, computer systems, and manufacturing equipment</li> <li>Revision of Process Water expiry</li> <li>Inclusion of (b) (4) (Table 7)</li> <li>Revision of process control computer system table (Table 10) to reflect process scales</li> <li>Addition of manufacturing equipment list for (b) (4) CX-024414, (b) (4), and (b) (4) mRNA-1273 LNP process scales</li> </ul>

Also included in this submission is a Response to CBER comments received on the Pre-EUA submission package on November 19, 2020.

If FDA has any questions, please do not hesitate to contact me directly at (b) (6) or at (b) (6) @modernatx.com.

This eCTD submission has been prepared by PPD Development, Inc. in full compliance with ICH and FDA guidance. The eCTD has been verified and confirmed to be virus and spyware free. PPD utilizes Palo Alto



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Traps v4.2.2. All technical questions should be directed to (b) (6) at PPD (b) (6) or email at (b) (6).

Yours Sincerely,

**Carlota Vinals** Digitally signed  
by Carlota Vinals  
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