

IND Number 19745
Sequence No. 0070

November 16, 2020

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Director, Office of Vaccines Research and Review
Center for Biologics Evaluation and Research
U.S. Food and Drug Administration
Document Control Center
10903 New Hampshire Avenue
WO71, G112
Silver Spring, MD 20993-0002

Submission Type: Information Amendment – Chemistry, Manufacturing and Control

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 provide analytical, Process Performance Qualification (PPQ) validation, and comparability assessment on lots for the (b) (4)

(b) (4) (ModernaTX, Inc. Norwood, MA), (b) (4) (Initial Scale B) of mRNA-1273 LNP manufacturing (ModernaTX, Inc. Norwood, MA), and (b) (4) (Scale A) of fill/finish manufacturing (Catalent Biologics, LLC Bloomington, IN) processes. In addition, the batch analysis, manufacturing process information and PPQ protocols for (b) (4) manufacturing (ModernaTX, Inc. Norwood, MA), (b) (4) (Scale B) of mRNA-1273 LNP manufacturing (ModernaTX, Inc. Norwood, MA) and (b) (4) (Scale B) of fill/finish manufacturing (Catalent Biologics, LLC Bloomington, IN) processes 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.4.1 {CX-024414}	Specification	<ul style="list-style-type: none"> Addition of validated SOP method numbers to specification table

(b) (4)

CTD Section		Changes
(b) (4)		
3.2.S.2.2 {mRNA-1273 LNP}	Description of Manufacturing Process and Process Controls	<ul style="list-style-type: none"> Addition manufacturing process and process controls information for (b) (4) (Scale B) of mRNA-1273 LNP
3.2.S.2.4 {mRNA-1273 LNP}	Control of Critical Steps and Intermediates	<ul style="list-style-type: none"> Revision of minor format/administrative errors Addition of alternate sanitization agent and limit for mixing skid Addition of footnote for mRNA preparation (thaw duration)
3.2.S.2.5 {mRNA-1273 LNP}	Process Validation and/or Evaluation	<ul style="list-style-type: none"> Addition of (b) (4) PPQ study information Addition of (b) (4) PPQ report and (b) (4) PPQ protocol
3.2.S.2.6 {mRNA-1273 LNP}	Manufacturing Process Development	<ul style="list-style-type: none"> Addition of lot detail for (b) (4) PPQ Lots Addition of mRNA-1273 LNP comparability assessment detail for (b) (4) PPQ lots and (b) (4) GMP lot. Addition of (b) (4) extended characterization report
3.2.S.4.1 {mRNA-1273 LNP}	Specification	<ul style="list-style-type: none"> Addition of validated SOP method numbers to specification table
3.2.S.4.4 {mRNA-1273 LNP}	Batch Analysis	<ul style="list-style-type: none"> Addition of (b) (4) PPQ and (b) (4) GMP batch data Revision of Certificates of Analysis attachment
3.2.P.2.3	Manufacturing Process Development	<ul style="list-style-type: none"> Addition of Scale B manufacture Addition of mRNA-1273 Drug Product lots 6007320004 and 6007320005 to Batch Genealogy Addition of data for extended processing duration hold times conducted on Catalent Scale A mRNA-1273 Drug product batches Addition of comparability between Scale A and Scale B at Catalent
3.2.P.3.1	Manufacturers	<ul style="list-style-type: none"> Addition of McKesson as distribution site for Emergency Use Authorization material
3.2.P.3.3	Description of Manufacturing Process and Process Controls	<ul style="list-style-type: none"> Revision to reflect Scale B manufacture Addition of (b) (4) Consumables
3.2.P.3.4	Control of critical Steps and Intermediates	<ul style="list-style-type: none"> Revision to reflect Scale B Controls Addition of in-process test descriptions and validations for mRNA Content and Visual Inspection
3.2.P.3.5	Process Validation and/or Evaluation	<ul style="list-style-type: none"> Addition of PPQ Protocol for Scale B manufacture inclusive of packaging and labeling activities Addition of revised PPQ Report for Scale A (Catalent) manufacture
3.2.P.5.1	Specifications	<ul style="list-style-type: none"> Revision to include validated method SOP#s
3.2.P.5.2	Analytical Procedures	<ul style="list-style-type: none"> Addition of reference to lipid reference materials (Administrative)
3.2.P.5.3	Validation of Analytical Procedures	<ul style="list-style-type: none"> Revised Attachment QC-MVR-0008 Methods validation Report of SOP-0999 Determination of RNA Concentration by IEX Chromatography for administrative revisions and corrections
3.2.P.5.4	Batch Analysis	<ul style="list-style-type: none"> Addition of Scale A (Norwood) GMP lot 6007520008 Addition of Scale A (Catalent) GMP lot 6007320004 (032H20)

CTD Section		Changes
		<ul style="list-style-type: none"> Addition of data for Scale B PPQ lot 6007320005 (011J20)
3.2.P.5.5	Characterization of Impurities	<ul style="list-style-type: none"> Addition of extractable leachable assessments for Scale A (Catalent) and Scale B mRNA-1273 Drug Product manufacture
3.2.P.6	Reference Standards	<ul style="list-style-type: none"> Addition of reference to lipid reference standards Removal of identity testing
3.2.P.7	Container Closure System	<ul style="list-style-type: none"> Addition of Certificate of Analysis for West Pharmaceutical Stopper Removal of (b) (4) technical drawings and Certificate of Analysis Addition of references to LoA for (b) (4)
3.2.P.8.1	Stability Summary and Conclusions	<ul style="list-style-type: none"> Implementation of statistical modeling for mRNA-1273 Drug Product to set minimum release limits and shelf life expiry periods, based on purity Addition of 6 month timepoint at -60°C to -90°C and -15°C to -25°C storage conditions for Lot DHM-47519 Addition of 6 month timepoint at -60°C to -90°C and -15°C to -25°C storage conditions for DHM-47516 Addition of 3 month timepoint at -60°C to -90°C, -15°C to -25°C, and 2°C to 8°C storage conditions for Lot 6007520001 Addition of 3 month timepoint at -60°C to -90°C, -15°C to -25°C, and 2°C to 8°C storage conditions for Lot 6007520002 Addition of 3 month timepoint at -60°C to -90°C, -15°C to -25°C, and 2°C to 8°C storage conditions for Lot 6007520003 Addition of 1 and 2 month timepoints at -60°C to -90°C and -15°C to -25°C storage conditions for Lot 6007520004 Addition of 1 month, 2 month and 76 days timepoints at 2°C to 8°C storage condition for Lot 6007520004 Addition of 24 hour and 72 hour timepoints at 23°C to 27°C storage condition for Lot 6007520004 Addition of 1 and 2 month timepoints at -60°C to -90°C storage condition for Lot 6007520005 Addition of 1 month timepoint at -60°C to -90°C (for 1 month) followed by 2°C to 8°C storage condition for Lot 6007520005 Addition of 1 and 2 month timepoints at -60°C to -90°C storage condition for Lot 6007520006 Addition of 1 month timepoint at -60°C to -90°C (for 1 month) followed by 2°C to 8°C storage condition for Lot 6007520006
3.2.P.8.3	Stability Data	
3.2.A.1 {Catalent}	Facilities and Equipment	<ul style="list-style-type: none"> Addition of batch numbering convention Addition of Catalent DMF#024888 section references Addition of details for mRNA-1273 Drug Product Manufacturing areas including HVAC, Equipment and Environmental Monitoring Program Addition of consumables control strategy

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 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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