

IND Number 19745
Sequence No. 0039

September 28, 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
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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 manufacturing, analytical and Process Performance Qualification (PPQ) validation documentation for the (b) (4) (b) (4) and mRNA-1273 LNP (b) (4) manufacturing processes at the ModernaTX, Inc. Norwood, MA manufacturing facility. In addition, PPQ activities for fill/finish were completed in August 2020 by ModernaTX, Inc.'s Contract Manufacturing partner, Catalent Biologics, LLC (Bloomington, IN, FEI 3005949964) for mRNA-1273 Drug Product (b) (4). The manufacturing, analytical and PPQ validation documentation is also provided in this submission.

The revised Module 3 sections, as described in the following table are being submitted including the final Certificates of Analysis for (b) (4) (b) (4) two additional mRNA-1273 lots, Lot 5006820006 and Lot 5006820007 and, three mRNA-1273 Drug Product PPQ lots filled at Catalent Biologics, Lot 6007320001, Lot 6007320002 and Lot 6007320003.

CTD Section	Changes
(b) (4)	
3.2.S.2.1 {mRNA-1273 LNP}	Manufacturer(s) <ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 LNP nomenclature (b) (4) This test was removed with the Specification revision to Version 2.0 (26 June 2020) Addition of “storage of mRAN-1273 LNP” to ModernatTX, Inc.
3.2.S.2.2 {mRNA-1273 LNP}	Description of Manufacturing Process and Process Controls <ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 LNP nomenclature Addition of Process Description by Unit Operation including process controls Additional detail added to Process Flow Diagram
3.2.S.2.4 {mRNA-1273 LNP}	Controls of Critical Steps and Intermediates <ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 LNP nomenclature Addition of Critical Process Parameter, (b) (4), in process holds, and hold time characterization studies
3.2.S.2.5 {mRNA-1273 LNP}	Process Validation and/or Evaluation <ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 LNP nomenclature Addition of the process validation and process performance qualification per unit operation for the mRNA-1273 LNP manufacturing process
3.2.S.2.6 {mRNA-1273 LNP}	Manufacturing Process Development <ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 LNP nomenclature Addition of process characterization studies Addition of analytical assessment across development phases Addition of summary of specification changes Addition of summary of analytical procedure changes
3.2.S.4.4 {mRNA-1273 LNP}	Batch Analyses <ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 LNP nomenclature Addition of mRNA-1273 LNP Lot 5006820007 release testing
3.2.S.6 {mRNA-1273 LNP}	Container Closure Systems <ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 LNP nomenclature

CTD Section		Changes
		<ul style="list-style-type: none"> Addition of materials of construction, specifications, suitability and extractable leachable information for the mRNA-1273 LNP container closure
3.2.S.7.1 {mRNA-1273 LNP}	Stability Summary and Conclusions	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 LNP nomenclature Addition of Stability protocol for PPQ lots Revision of extension of use period strategy (b) (4)
3.2.S.7.3 {mRNA-1273 LNP}	Stability Data	
3.2.P.1	Description and Composition of the Drug Product	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Addition of Drug Product Presentation table Revision to unit formula for 6.3 mL fill volume Revision of long-term storage condition from -60°C – 90°C to -15°C to -25°C
3.2.P.2.2	Drug Product	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Addition of historical formulation development and justification
3.2.P.2.3	Manufacturing Process Development	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Addition of process characterization studies Addition of analytical assessment across development phases Addition of summary of specification changes Addition of summary of analytical procedure changes
3.2.P.2.5	Microbiological Attributes	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Addition of container closure integrity qualification and microbiological growth promotion study
3.2.P.3.1	Manufacturer(s)	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Addition of Emergency Use Authorization (EUA) supply responsibilities Addition of Catalent Indiana, LLC as addition Fill/Finish, packaging, labelling, and sterility testing facility for clinical and EUA supply
3.2.P.3.2	Batch Formula	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Revision of batch size and formula to a representative (b) (4) scale Addition of mRNA-1273 Drug Product Batch Manufacturing Formula
3.2.P.3.3	Description of Manufacturing Process and Process Controls	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Revision of manufacturing process and process controls to reflect fill/finish activities at Catalent Indiana LLC. Addition of vial conditioning freeze at -40°C Revision of long-term storage from -60°C – 90°C to -15°C to -25°C
3.2.P.3.4	Control of Critical Steps and Intermediates	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Addition of Critical Process Parameters, (b) (4) and critical in process controls
3.2.P.3.5	Process Validation	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Addition of process performance qualification for (b) (4) Addition of Aseptic Manufacturing Validation for (b) (4) at Catalent Indiana LLC Addition of environmental monitoring program at Catalent Indiana, LLC
3.2.P.4.1	Specifications	<ul style="list-style-type: none"> Administrative Change to remove “LS” from mRNA-1273 nomenclature Revision of compendia references for Sucrose and Tris Addition of Advantor (b) (4) Revision of specifications for Tris-HCL

CTD Section		Changes
		<ul style="list-style-type: none"> Removal of as supplier of Tris-HCL
3.2.P.5.1	Specifications	<ul style="list-style-type: none"> Administrative Change to remove "LS" from mRNA-1273 nomenclature Revision of specifications for RNA Content, Purity, lipid impurities and container content
3.2.P.5.4	Batch Analyses	<ul style="list-style-type: none"> Addition PPQ lots 6007320001, 6007320002 and 6007320003
3.2.P.7	Container Closure System	<ul style="list-style-type: none"> Administrative Change to remove "LS" from mRNA-1273 nomenclature Addition of specifications and extractable leachable information for the mRNA-1273 container closure
3.2.P.8.1	Stability Summary and Conclusion	<ul style="list-style-type: none"> Administrative Change to remove "LS" from mRNA-1273 nomenclature Addition of stability protocols for Lot 6007520007 (b) (4) lot 6007320001 (Catalent) and 6007320002 (Catalent) and 6007320003 (Catalent) Addition 4 and 5 mo data at 2°C to 8°C for lot DHM-47519 and for lot DHM-47516 Addition 2 mo data at -60°C to -90°C -15°C to -25°C for lot 6007520001, for lot 6007520002 and for lot 6007520003 Addition 2 mo data and 76 day at 2°C to 8°C for lot 6007520001, for lot 6007520002 and for lot 6007520003 Addition of clinical in-use compatibility data for lot 6007520007 (0.2mg/mL)
3.2.P.8.3	Stability Data	
3.2.A.1 {ModernaTX, Inc. - Norwood}	Facilities and Equipment	<ul style="list-style-type: none"> Addition of detail for ModernaTX, Inc. Norwood facility's manufacturing areas, utilities, computer systems, equipment, cleaning and product changeover, environmental monitoring, Quality Control laboratory, and warehouse and supply chain facilities/locations Removal of reference to ModernaTX, Inc. Norwood facility Site Master File
3.2.A.1 {Catalent}	Facilities and Equipment	<ul style="list-style-type: none"> Addition of Facilities and Equipment information pertaining to Catalent Indiana, LLC.

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

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