

## FDA Briefing Document

<b>Active Substance:</b>	mRNA that encodes for the pre-fusion stabilized Spike protein of 2019-novel Coronavirus (SARS-CoV-2).
<b>Intended Indication(s):</b>	mRNA-1273 is a vaccine indicated for the prevention of disease caused by SARS-CoV-2
<b>Applicant:</b>	ModernaTX, Inc. 200 Technology Square Cambridge, MA 02139 USA
<b>Version:</b>	1
<b>Date:</b>	September 04, 2020

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## 1. SUMMARY

### 1.1. Product Name(s) and Application Number

mRNA-1273 Drug Product, a lipid-encapsulated mRNA-based prophylactic vaccine encoding the pre-fusion stabilized spike (S) glycoprotein of the SARS-CoV-2 virus. The Investigational New Drug (IND) Application number is IND# 19745.

### 1.2. Chemical Name, Established Name and/or Structure

mRNA-1273 Drug Product is a lipid nanoparticle (LNP) dispersion containing an mRNA (CX-024414) and four lipids: SM-102 (a custom-manufactured, ionizable lipid); PEG2000-DMG; cholesterol and 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC).

### 1.3. Proposed Indication(s) or Context of Product Development

mRNA-1273 Drug Product is a vaccine indicated for the prevention of the disease caused by SARS-CoV-2.

### 1.4. Background

The Sponsor is collaborating with the Biomedical Advanced Research and Development Authority (BARDA) and the National Institute of Allergy and Infectious Diseases (NIAID) to develop an mRNA-based vaccine, mRNA-1273, in response to the current COVID-19 declared Public Health Emergency (PHE). The Sponsor is working to expedite the development of the mRNA-1273 vaccine and believes that early and frequent engagement and guidance from the Agency will be critical to accomplish this goal.

### 1.5. Introduction

In consideration of the resources and time required to bring a mass-produced vaccine to market, the Sponsor is executing its establishment of the licensable manufacturing processes and corresponding PPQ strategy in two phases. The following table (Table 1) provides an overview of the two manufacturing process scales.

**Table 1: Summary of mRNA-1273 Manufacturing Process Scales**

Process	Scale A PPQ		Scale B PPQ	
	Site	Nominal Batch Scale	Site	Nominal Batch Scale

(b) (4)

- a) Initial scale at Lonza will be at (b) (4) to gain manufacturing experience (Initial Lonza Scale B) and will be part of PPQ activities.  
(b) (4) scale manufacture will not be conducted at ModernaTX, Inc.
- b) Initial scale at Moderna will be at (b) (4) to gain manufacturing experience (Initial Norwood Scale B) and will be part of PPQ activities.  
(b) (4) scale manufacture will not be conducted at Lonza.
- c) Initial scale at Moderna will be at (b) (4) to gain manufacturing experience (Initial Norwood Scale B) and will be part of PPQ activities.  
(b) (4) scale manufacture will not be conducted at Lonza.

The Sponsor has completed Scale A Drug Substance (b) (4) process validation for mRNA-1273 (Table 1) in August 2020 at its GMP manufacturing facility in Norwood, MA [refer to mRNA-1273 Process Validation Master Plan (PVMP)]. Scale A finished product was completed at Catalent Biologics, in August 2020. In addition to this initial validated commercial scale, the Sponsor is planning to validate a second commercial scale, Scale B, with three, equivalent drug substance production trains in Norwood. The Scale B drug product will also be manufactured and filled at Catalent Biologics in Bloomington Indiana. Lonza Biologics, Inc. has been contracted to provide additional commercial production capacity for the mRNA-1273 Drug Substance, adding one process train. The production scale at Lonza is equivalent to the Norwood Scale B (b) (4) manufacturing processes. See Table 1 for production history and plans.

The Sponsor manufactured Scale A (b) (4) vial drug product lots at the Norwood facility for clinical supply. The Sponsor's Norwood, MA drug product manufacturing site or filling equipment has not been used nor is it intended to be used in the future for the commercial manufacture of the multiple-dose vial mRNA-1273 Drug Product. As noted earlier, Commercial manufacture of the multiple dose vial mRNA-1273 Drug Product will occur at Catalent Biologics, LLC, Bloomington, IN site. Scale A (Catalent fill) PPQ activities have been completed. One flexible filling line (b) (4) at Catalent Biologics was used to manufacture the nominal (b) (4) vial filling capacity (Scale A). PPQ activities are being planned to conduct PPQs for the mRNA-1273 Drug Product with up to a (b) (4) vial capacity (Scale B) on the (b) (4) filling line. Both CMOs, Lonza and Catalent, were selected as contract manufacturing partners based upon their extensive commercial experience and regulatory history along with routine Health Authority inspections.

As per electronic correspondence between Jennifer White, ModernaTX, Inc. Senior Vice President Global Quality and (b) (6), FDA on August 4, 2020, the Sponsor is requesting a Type C meeting teleconference to review the list of general overview items in anticipation of a pre-emergency use FDA visit. The Sponsor would like to provide the Agency with details on the manufacturing history and the future plans, the facility and laboratory upgrades, the existing quality systems and preparation activities underway. Our strategy for validation, testing and related controls will be presented in order for the Agency to assess the GMP and scientific feasibility of the batches slated for EUA consideration. The Sponsor would also like to discuss other quality system related topics, such as lot release requirements, as part of that meeting.

## 1.6 Proposed Date, Agenda and Attendees

ModernaTX, Inc. proposes a video teleconference meeting in the morning or afternoon on any of the following available dates:

September 14, September 15 or September 16, 2020

**Table 2: Proposed Agenda**

Meeting duration requested: 60 minutes

Topic	Estimated Duration
Introduction of meeting participants	5 minutes
Discussion	50 minutes
Summary of discussion and wrap-up	5 minutes

The following sponsor proposed participants will attend the Type C teleconference meeting:

**Table 3: Proposed Sponsor Participants**

Name	Title
(b) (6)	Chief Technical Operations and Quality Officer
(b) (6)	Senior Vice President, US Manufacturing
Jennifer White	Senior Vice President, Global Quality
Charbel Haber	Senior Vice President, Regulatory Affairs
Paul Dawidczyk	Vice President, Regulatory Affairs CMC
(b) (6)	Senior Director, Facilities and Engineering
Nedim Altaras	Senior Vice President, Technical Development
(b) (6)	Vice President, Manufacturing Science and Technology
(b) (6)	Vice President, CMC Project Management
(b) (6)	Consultant, Quality
Appropriate BARDA attendees	

### Requested FDA Participants

In addition of requested representatives from Office of Vaccines Research and Review (OVRR) CMC- Reviewer and Division of Manufacturing and Product Quality (DMPQ), ModernaTX, Inc. requests that the Agency determines the appropriate FDA attendees for the meeting based on the information provided and informs ModernaTX, Inc. of FDA attendees.

## 2. MANUFACTURING FACILITIES DESCRIPTIONS

The following sections contain quality information on Moderna facilities and anticipated commercial manufacturing and analytical testing sites.

**Table 4: mRNA-1273 Manufacturing and Analytical Testing Sites (Current and Anticipated)**

Company	Address	Activity	Current/Anticipated Commercial
ModernaTX, Inc.	One Moderna Way Norwood, MA 02062 United States	(b) (4)	Current/Anticipated <sup>a)</sup> <ul style="list-style-type: none"> <li>Scale A (CX-024414 mRNA (b) (4) mRNA-1273 LNP (b) (4) mRNA-1273 DP (b) (4) ) completed July/August 2020.</li> <li>Initial Scale B (CX-024414 mRNA (b) (4) mRNA-1273 LNP (b) (4) ) anticipated start late August 2020.</li> <li>Scale B (b) (4) mRNA-1273 LNP (b) (4) , mRNA-1273 LNP (b) (4) anticipated start October 2020.</li> </ul>
Lonza Biologics, Inc. (FEI# 3001451441)	101 International Drive, Portsmouth, NH 03801 United States		Anticipated: <ul style="list-style-type: none"> <li>Initial Scale B (CX-024414 mRNA (b) (4) ) initiated August 2020.</li> <li>Scale B (b) (4) mRNA-1273 LNP (b) (4) anticipated start October 2020.</li> </ul>
Catalent Biologics, LLC (FEI# 3005949964)	1300 South Patterson Drive Bloomington, IN 47403 United States		Anticipated: <ul style="list-style-type: none"> <li>Scale A mRNA-1273 DP (b) (4) ) completed August 2020.</li> <li>Scale B (mRNA-1273 DP (b) (4) ) anticipated start September 2020.</li> </ul>
ModernaTX, Inc.	210 Rustcraft Road Dedham, MA 02026 United States		Anticipated: <ul style="list-style-type: none"> <li>Renovation, commissioning and qualification activities underway, anticipated start October/November 2020</li> </ul>
Associates of Cape Cod, Inc. (FEI# 1219145)	124 Bernard St. Jean Drive East Falmouth, MA 02536 United States		Current/Anticipated
(b) (4)			

a) mRNA-1273 DP manufactured at ModernaTX, Inc. in Norwood, MA, is not intended for EUA or commercial distribution

## 2.1. ModernaTX, Inc. (Moderna)

Moderna's Manufacturing Technology Center's multi-product manufacturing and testing site (for mRNA based products) is located at One Moderna Way, Norwood, MA, USA, 02062 and produces DNA plasmid, mRNA, lipid nanoparticle (LNP), clinical trial drug product (DP). The facility consists of approximately (b) (4) divided between two levels. The manufacturing area is located on the (b) (4) of the facility and occupies approximately (b) (4). The area is supported by adjacent Quality Control (QC) Laboratories, and a Supply Chain area consisting of warehouse storage, shipping and receiving. Other areas supporting manufacturing include utility areas, general amenities, research and development laboratories offices, and circulation spaces. The (b) (4) of the facility consists of research and development laboratories, pre-clinical manufacturing, utility areas, offices, amenities and circulation spaces.

There is a second building at the Manufacturing Technology Center at 200 Tech Drive that houses administrative offices and research and development laboratories. No current GMP activities occur here, however in the future warehouse activities may be performed in this building. A [site map](#) of the Moderna campus is provided as an attachment. The number of Moderna Norwood (One Moderna Way) staff level in the areas of Production, Quality Unit and Technical Support are listed in [Table 5](#).

**Table 5: ModernaTX, Inc. Norwood Staff Level in Support of cGMP Operations<sup>(a)</sup>**

(b) (4)



### 2.1.1 Overview of the mRNA-1273 Drug Product Manufacturing Processes

An overview of the process flow diagram for mRNA-1273 Drug Substance and Drug Product manufacturing process is provided in [Figure 1](#).

(b) (4)



(b) (4)

Moderna considers this the completion of the Drug Substance process. For the Drug Product, the mRNA-lipid complex [lipid nanoparticle (LNP)] dispersion is thawed, pooled, clarification filtered and diluted with a dilution buffer to the target mRNA-1273 concentration. The bulk mRNA-lipid complex solution is (redundant) sterile filtered and aseptically filled into 10R vials.

**Figure 1: mRNA-1273 Manufacturing Process Scheme**

(b) (4)



**2.1.1.1 Manufacture of CX-024414 (mRNA)**

(b) (4)



**Figure 2: CX-024414 mRNA Manufacturing Scheme**

(b) (4)



(b) (4)

(b) (4)

(b) (4)



(b) (4)



### **2.1.1.3     Manufacture of mRNA-1273 Lipid Nanoparticle (LNP)**

(b) (4)



An overview of the process flow diagram for mRNA-1273 LNP manufacturing process is provided in [Figure 4](#).

**Figure 4: mRNA-1273 LNP Manufacturing Process Scheme**

(b) (4)



**2.1.1.4 Manufacture of mRNA-1273 Drug Product**

(b) (4)



adjusted with a dilution buffer comprising 20 mM Tris and 87 mg/mL sucrose, pH 7.5, to achieve the target mRNA content (b) (4) The resultant bulk product solution is sampled for pre- filtration bioburden and tested with a specification of (b) (4)

(b) (4)



(b) (4)

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The process flow diagram for mRNA-1273 Drug Product manufacturing process is provided in [Figure 5](#).

**Figure 5: mRNA-1273 Drug Product Manufacturing Process Scheme**

(b) (4)

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**2.1.1.5 Facility Modifications**

(b) (4)

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**Table 6: Moderna Facility Modifications to Support mRNA-1273 Manufacturing Processes**




(b) (4)



## **2.1.2 Multi-Use Considerations**

### **2.1.2.1 Procedures to Prevent Contamination and Cross-Contamination**

The Moderna Norwood facility operates as a multi-product facility for mRNA based products. Access to the manufacturing areas is controlled by a card key system and limited to authorized personnel. The clean rooms are designed to provide a controlled environment for production of bulk biopharmaceuticals. Room pressurization, airlocks and gown rooms facilitate product/process separation and containment. The surface finishes in the production areas are consistent with the intended function of the area and were designed for durability and ease of cleaning. (b) (4)



(b) (4)



(b) (4)

#### 2.1.2.2 Cleaning Validation

The mRNA-1273 manufacturing processes use predominantly use single process equipment and containers. (b) (4)

Cleaning verification is ongoing and cleaning validation is underway for the reusable equipment used in these processes. Cleaning verification is performed between products on re-usable equipment and where cleaning validation is not complete. The [Cleaning Validation Master Plan](#) for the Norwood Facility for Scale A is provided, the Cleaning Validation Master Plan for Scale B is under development. The [Cleaning Validation Policy](#) is provided as a reference. The objective of cleaning verification/validation is to demonstrate that the equipment is consistently cleaned of product, detergent/cleaning solution and microbial residue as per specification, prior to each use. Clean and dirty hold times will be established.

Each facility involved in the production of each stage in the process will be responsible for executing cleaning validation studies in accordance with Moderna's validation requirements, acceptance criteria and limits, using validated analytical methods. The requirements will be set forth in the Quality Agreements for each contract manufacturer. Cleaning validation encompasses multiple aspects including, but not limited to:

- Carryover of product.
- Carryover of detergent/cleaning solution.
- Microbial control (effectiveness of disinfecting solutions, rotation of disinfecting agent).
- Visual cleanliness.
- Dirty hold time, prior to cleaning.
- Clean hold time, prior to use.

Until validation is completed, cleaning verification will be performed for all equipment at the predefined steps and the data will be evaluated as part of the release process. Excursions will be investigated as per the requirements in Moderna's quality systems.

#### 2.1.2.3 Manufacturing Equipment and Equipment Cleaning

(b) (4)

(b) (4)

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**Table 7: Major Equipment Used for mRNA-1273 Manufacturing**

(b) (4)

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Reusable Equipment used for mRNA-1273 manufacturing that has product contact is provided in [Table 8](#) below. The equipment undergoes chemical cleaning and sanitization.


**Table 8: Major Reusable Equipment (Product Contact) Used for mRNA-1273 Manufacturing**


(b) (4)



#### **2.1.2.4 Environmental Monitoring**

The Moderna Environmental Monitoring Program for the manufacturing area is performed according to defined SOPs. Routine environmental monitoring consists of (b) (4)



 to the extent possible sampling will be scheduled in a manner that accounts for multiple shifts and operations.

**Table 9: Sample Frequency**

(b) (4)



Alert and action limits for surface and air monitoring are provided in [Table 10](#) and [Table 11](#). [Sample Site Maps and Descriptions](#) are provided for reference.

**Table 10: Acceptance Criteria Microbial Contamination**

(b) (4)



**Table 11: Total Particulate Air Levels**

(b) (4)



### **2.1.3 Manufacturing Utilities**

#### **2.1.3.1 Heating, Ventilation and Air Conditioning (HVAC) Systems**

(b) (4)



(b) (4)



**Table 12: Norwood, MA Facility (One Moderna Way) Manufacturing Area Classification**  
(b) (4)



#### **2.1.3.2. Water Systems**

(b) (4)



(b) (4)

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**Table 13: WFI Specifications**

(b) (4)

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### **2.1.3.3 Compressed Air and Process Gas Systems**

(b) (4)

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#### 2.1.3.4 Nitrogen

(b) (4)



#### 2.1.3.5 Carbon Dioxide (CO<sub>2</sub>)

(b) (4)



#### 2.1.3.6 Oxygen

(b) (4)



### 2.1.4 Facilities, Utilities, Systems, and Equipment (FUSE) Qualification/Validation

Moderna has established a [Validation Master Plan](#) (VMP) to provide an outline of the Commissioning, Qualification, and Validation (CQV) strategy, activities, sequence, role and responsibilities, and practices from mechanical completion through validation/equipment turnover. The CQV philosophy is focused on the use of quality management tools to ensure that critical systems are suitable for use and maintained in compliance to validated limits. The VMP provides an overview of the planning, structure, change control, and documentation for validation processes at the manufacturing facility.

The overall qualification approach is risk-based according to ASTM E2500, and utilizes the “Life Cycle” approach for commissioning and qualification. Each user requirement is evaluated against different failure scenarios and possible risks that may impact product quality or patient safety. The approach allows the validation effort to focus on the user requirements and define corresponding

critical aspects of the FUSE that pose risks that can be mitigated via testing throughout the CQV process. (b) (4)

### 2.1.5 Media Fill Overview

(b) (4)

## 2.2. Lonza Biologics, Inc.

As noted in [Section 1.5](#) and per FDA Briefing Document (IND 19745 SN0005 Dated 23 June 2020), for the second manufacturing phase, Scale B, the Moderna will scale-up the (b) (4) manufacturing processes at Norwood, MA and utilize Lonza Biologics, Inc for additional manufacturing capacity. Lonza Biologics facility specific information is contained in Lonza Biologics (b) (4). (Refer to [Letter of Authorization from Lonza Biologics](#)).

## 2.3. Catalent Biologics, LLC

As noted in [Section 1.5](#), Catalent Biologics, LLC has completed the validation of the first manufacturing phase, Scale A, (b) (4) multi-dose vials, in August 2020. For further additional drug product manufacturing capacity, Catalent Biologics, LLC is performing the second manufacturing phase, Scale B mid/late August 2020. Catalent Biologics facility specific information is contained in Catalent Biologics (b) (4). (Refer to [Letter of Authorization from Catalent](#)).

## 2.4. Current and Future Analytical Sites

### 2.4.1 ModernaTX, Inc. Quality Control Laboratory (Norwood, MA)

The Quality Control (QC) Laboratories are located on the (b) (4) of the One Moderna Way Norwood, MA Facility. The laboratories consist of Microbiology, Raw Materials, Bioassay, Chemistry, Sample Management, and Stability departments. Moderna's Quality Control department has responsibility for the following activities:

- Sampling and testing of Raw Materials per effective specifications
- Sample distribution to contract testing laboratories
- Environmental monitoring, testing and trending for the GMP facility and utilities
- Method qualifications and validations
- In-process, Drug Substance, Lipid Nanoparticle, Drug Product testing for GMP production batches
- Generation of raw material and product specifications
- Generation of product certificates of analysis
- Stability testing and assignment of product expiration dates and extensions
- Contract lab oversight for GMP testing and method qualification
- Sampling and storage of retain samples for GMP batches

The testing laboratories within the Moderna facility have been appropriately commissioned. Equipment is qualified prior to use and meet current GMP requirements. The QC Microbiology Laboratory testing facilities are segregated from the Chemistry Laboratories. The Microbiology Laboratory is constructed to ensure adequate utilities, space and environmental conditions to provide microbial testing in a manner consistent with current GMP. The QC sterility testing area has a separate Air Handling Unit from that supplying the QC Chemistry Laboratory. The HVAC systems servicing the QC Microbiology Laboratory area have been appropriately qualified and demonstrates that the system operates according to design specifications and is capable of maintaining the facility within the design parameters. The facility design incorporated isolated areas for microbiological-specific activities such as sample plating and microbial identification testing to reduce the potential for cross-contamination. Surfaces were designed to be easily cleanable.

All equipment meets the design and operating parameters for its intended use. Examples of the major and ancillary equipment in the QC Laboratories are listed in [Table 15](#).

**Table 15: Major and Ancillary Laboratory Equipment**

(b) (4)



#### **2.4.2 ModernaTX, Inc. Quality Control Laboratory (Dedham, MA)**

To increase testing capacity, Moderna Quality Control will be expanding its operations to an additional, qualified-laboratory space in Dedham, MA, approximately 3 miles from the existing lab. The new QC laboratory is located at 210 Rustcraft Road, Dedham, MA 02026, USA and will be registered under the same Quality Management System as Moderna Technology Center.

#### **2.4.3 Associates of Cape Cod, Inc.**

Associates of Cape Cod is located at 124 Bernard St. Jean Drive, East Falmouth, MA 02536, USA. Associates of Cape Cod currently and will continue to perform bacterial endotoxin testing for release and stability for (b) (4) mRNA-1273 Drug Product. Quality agreements between Moderna and Associates of Cape Cod are in place.

(b) (4)



## 2.5 Warehouse /Supply Chain Storage

(b) (4)



### 3. LIST OF PROPOSED QUESTIONS

#### 3.1. Question 1

Quality of materials is assured through a rigorous system consisting of supplier evaluation, supplier qualification, audits, quality agreements, incoming goods testing, internal release procedure, package selection, shipping, storage conditions, expiry dates, and/or sterility requirements, based on the risk and criticality of supplier and/or material.

*Does the Agency agree with ModernaTX, Inc. Raw Material Strategy?*

#### Sponsor's Position

Raw materials are received from qualified suppliers. The supplier qualification process demonstrates that the supplier has an effective and acceptable Quality Management System in place and that their supplied raw materials can meet the minimum quality requirements of the process. Qualified suppliers have been assessed and qualified using a supplier risk level review as well as audit requirements based on the materials to be sourced from the supplier. Supplier performance is maintained and monitored through routine surveillance audits, periodic re-verification of release assay performance, quality agreements, and change notification agreements based on supplier risk level.

The risks related to quality will drive the level of criticality. The risk factors that drive the levels of criticality with regards to quality are composed of:

- The type of material and its origin (chemical, biological, complexity, animal/human origin);
- Where it is used in the process and its functionality;
- Contact between RM and DS/DP as well as process time;
- Manufacturing process capabilities to reduce its amount to acceptable levels;
- Its variability in terms of quality under the standard manufacturing process used by suppliers.
- The quality agreement-audited quality systems, and change control notification.
- The storage condition, use and re-use.

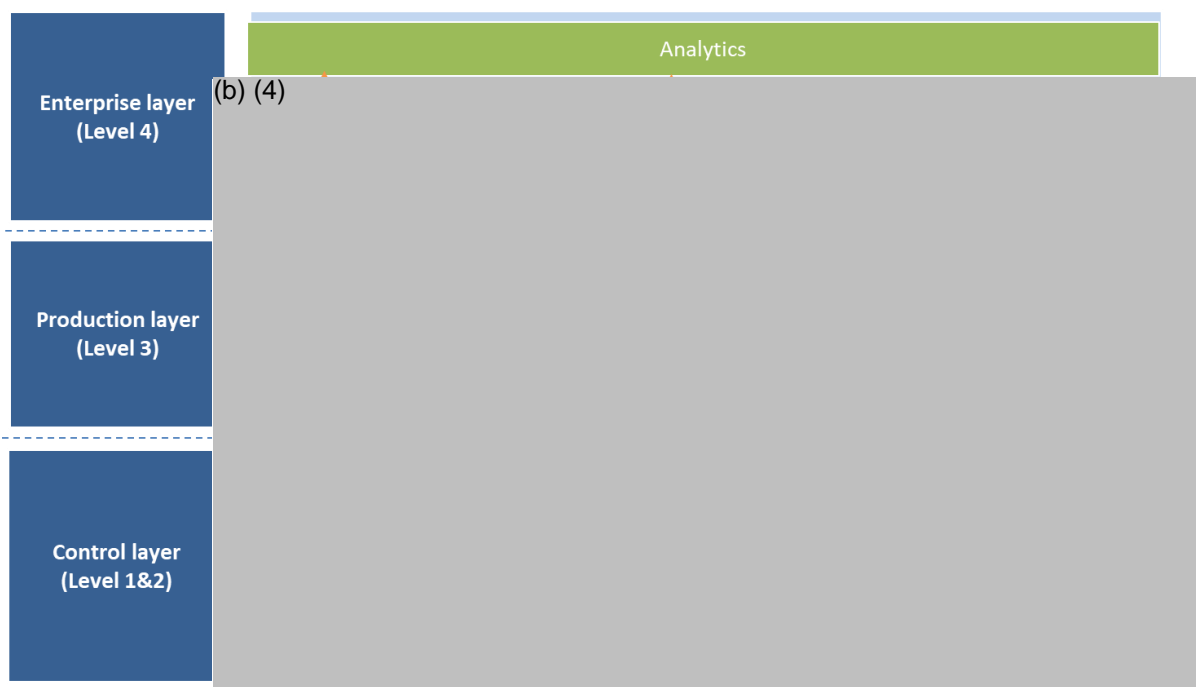
Currently, incoming raw materials are released based on the Certificate of Acceptance and/or incoming goods testing. The Certificate of Acceptance and/or testing results are compared against the material specification prior to material release. Material identification testing is also performed.

Moderna is currently qualifying raw materials from approved vendors concurrently with manufacturing process validation. A raw material qualification master plan guiding the raw material qualification is in-progress. The Raw Material qualification process is procedurally driven utilizing 3 unique vendor lots to qualify a material from a vendor and requiring periodic requalification. The testing strategy and prioritization is based on completed risk assessments based on purpose of the unit operation where the raw material is used and the proximity of that unit operation to the final drug product.

### 3.2. Question 2

Moderna has designed, validated and deployed a native digital system landscape to support the manufacturing, testing, release and distribution of mRNA-1273. The objective of the design is to improve compliance, control and repeatability. By removing duplicative data transcription steps, reducing manual equipment inputs, and capturing all process data electronically, data integrity is assured. Reviews of manual operations and exceptions provide alerts as to when process deviations occurred, allowing for timely notification to Quality Assurance, investigation and resolution. Material allocations, manufacturing operations, in process and quality control sampling and testing, quality reviews, disposition actions and distribution are integrated onto a qualified infrastructure, based on ISA 95/88. Thus, there are limited paper records associated with the entire workflow. [Figure 6](#) depicts the specific systems, supporting infrastructure components and information flows.

**Figure 6: Digital Landscape Diagram**



*Does the Agency agree to accept CoAs, protocols, batch summaries, and exception reports for its review of the lot release program without the additional generation of paper records?*

#### Sponsor's Position:

#### **Qualification of Systems**

Electronic systems are validated following *POL-0022, Computer System Validation Policy* and *SOP-0055, Computer System Validation Lifecycle* ([Table 16](#)).

**Table 16: Qualified Electronic Systems**

(b) (4)



**Material Control**

(b) (4)



**Manufacturing Operations**

The manufacturing digital landscape includes the integration of the ISA-95 manufacturing operation management and control layers. Operators follow steps in the (b) (4) (b) (4) to execute the process. Electronic batch records in the (b) (4) include integrated controls to track materials, equipment and samples. Product specific processing parameters are defined in each product's technology transfer document per SOP-0543, Technology Transfer Procedure. These operating parameters are configured in the (b) (4) system and will electronically control the equipment during each respective manufacturing operation. Exceptions or deviations, are electronically captured, reviewed and approved by Quality Assurance per SOP-0523, Electronic Batch Record (EBR) Review Procedure.

Unit operations for each electronic batch record are qualified. Performance Qualification includes end-to-end batch record execution as shown in [Figure 7](#). Changes to electronic batch records are managed following SOP-0286, GXP Computer Systems Change Management and SOP-0034, Change Control. Electronic batch records are issued following SOP-0277, Creating and Issuing Process Orders in (b) (4).

## Figure 7: Batch Record Qualification and Issuance

(b) (4)



### Quality Control

Approved sampling plans are stored in the (b) (4) system and integrated with the electronic batch record. Samples collected during processing are tested and approved in (b) (4) in accordance with the approved testing method. Test results where required for batch record calculations are electronically submitted to the (b) (4) system to allow for forward processing.

Laboratory bench-top workstations are secured with (b) (4) (b) (4) system. (b) (4) allows analyst to access only the analytical software required for test execution. When instrument data is generated by the analytical software, the (b) (4) transfers the data to a centralized electronic vault. Access to raw data on the workstation is restricted and includes an audit trail and electronic chain of custody. A Certificate of Analysis (CoA) is generated and approved electronically in the document management system. OOS/OOT data is investigated as per SOP-0033 and SOP-0028, Out of Specification and Deviations, respectively, and all results are maintained as part of the data file.

Environmental and water monitoring sample plans are stored in (b) (4) Results are reported as required and any excursion flagged for investigation prior to batch release. Trend reports are generated and utilized for periodic reviews of the effectiveness of environmental controls.

### Product Disposition

Table 17 provides current and future outputs for batch product disposition.

**Table 17: Product Release** Moderna, would you prefer Minor deletion here?

Process	Current Output	Governing Procedure	Future State Output
Batch Record Issuance	(b) (4)		
Batch Record Review			
Testing			
Environmental Monitoring			
Disposition of GMP Batches			

### 3.3. Question 3

Moderna is planning to perform shipping validation activities for commercial shipments of mRNA-1273 products being manufactured at Moderna and Moderna associated CMO sites. The mRNA-1273 LNP will be frozen and subsequently dispatched to filling sites for final processing. The final labeled drug product will be shipped from the fill site to designated depots for commercial distribution.

Shipment of mRNA-1273 products must ensure controlled conditions across the cold chain to maintain product quality attributes. Shipments will be performed either via road transportation or a combination of road and air transportation. Moderna has developed a shipping validation master plan and associated shipping protocols that will demonstrate anticipated environmental factors and shipping methods do not have an impact on the quality, safety, and efficacy of the product.

***Does the Agency agree with ModernaTX, Inc. Shipping Validation Strategy?***

#### **Sponsor's Position:**

The Moderna shipping validation strategy will follow the principles of lifecycle validation, comprising the activities depicted in [Figure 8](#).

**Figure 8: Shipping Validation Strategy**



The shipping requirements for mRNA-1273 LNP and mRNA-1273 labelled drug product are provided in further detail in the [Moderna mRNA-1273 Shipping Validation Master Plan](#). The shipping lanes are also provided in [Table 18](#) below.

**Table 18: mRNA-1273 Shipping Lanes**

mRNA-1273 LNP		
Shipping Lanes	From	To
	Moderna (MA, USA)	Catalent (IN, USA)
	Lonza (NH, USA)	Catalent (IN, USA)
mRNA-1273 Drug Product		
Shipping Lanes	From	To
	Catalent (IN, USA)	(b) (4)
	Catalent (IN, USA)	(b) (4)
	(b) (4)	(b) (4)

First, design testing/assessment will be performed to identify the shipping system required to meet the product shipping conditions. Design assessment includes items such as (b) (4) (b) (4) to define qualification requirements and review of existing vendor qualification packages. Product shipping characterization studies are ongoing to demonstrate product robustness against anticipated stresses during transportation. Design testing/assessment activities will be summarized in the (b) (4) where the outcomes will be used to assess transport risk to product quality.

The shippers identified as shipping systems for mRNA-1273 LNP and mRNA-1273 drug product are industrially available and have been identified following review of vendor qualification packages and/or protocols. Vendor design and qualification documents were reviewed to assess functionality against the shipping conditions identified. Where vendor qualification data is

unavailable or insufficient, Moderna is engaging with the shipper vendor to execute a qualification protocol against Moderna's requirements. Vendor qualification data will be accessible through vendor reports and will be summarized in Moderna's PQ protocol.

(b) (4)



(b) (4)



It is anticipated that the complete shipping validation program will be finalized at the point of BLA submission.





















































































































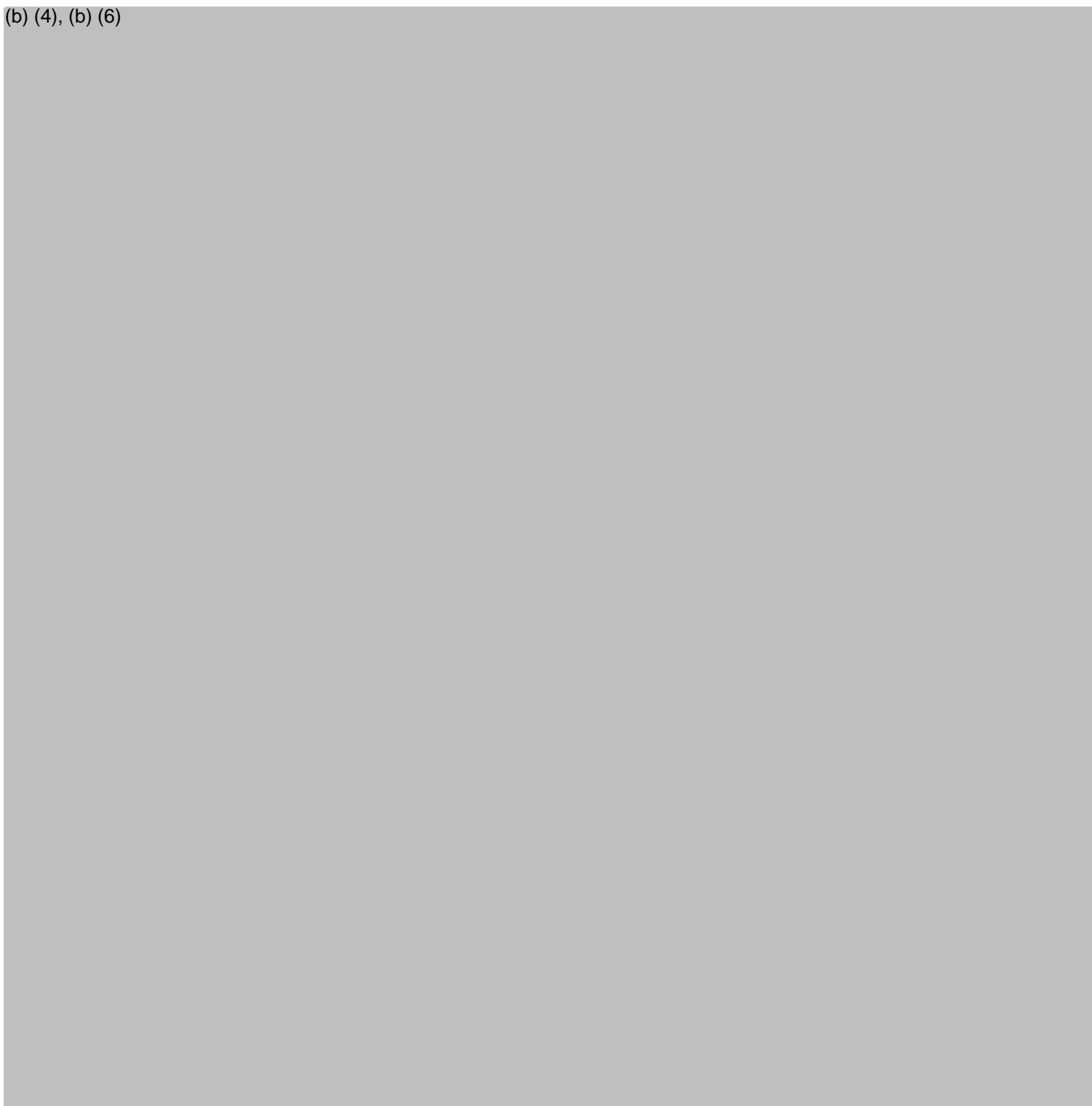








(b) (4), (b) (6)



(b) (4), (b) (6)

