DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue Stoneham, MA 02180 (781)587-7500 Fax:(781)587-7556 Email: orabioinspectionalcorrespondence@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	09/11/2023-09/21/2023 FEI NUMBER 3014937058

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED	
Ms. Kathrin Knauf, Vice President, Site Head	
TO: FIRM NAME ModernaTX, Inc.	STREET ADDRESS One Moderna Way
CITY, STATE, ZIP CODE, COUNTRY Norwood, MA 02062-1568	TYPE ESTABLISHMENT INSPECTED Licensed Biological Drug Substance Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1:

Equipment utilized for drug substance manufacturing are not cleaned properly prior to its usage.

Specifically, your firm does not ensure that the equipment used for drug substance manufacturing are appropriately cleaned prior to the manufacturing of mRNA-1273 drug substance. Your written procedure, SOP-0417, version 10, effective on 01Dec2021 through the current version 16.0, effective on 10Jun2023, entitled as "Manufacturing Room Product Changeover – Norwood" allows the release of manufacturing equipment without confirming the cleaning verification test results for bioburden and endotoxin prior to the usage for subsequent batch manufacturing. Your firm has identified bioburden failures on cleaning verification samples collected from (b) (4), Equipment ID# MIX-1805, MIX-7807, MIX-7805, and MIX-3807, which were utilized for manufacturing drug substance batches 5007522046, 5007522017, 5007522119, 5007522125, 5007522131, 5007522135, 5007522136, 5009222022 and these batches were released.

OBSERVATION 2

Cleaning Validation studies of non-dedicated manufacturing equipment did not include challenges with actual conditions used in routine manufacturing processes. Your firm's Cleaning Validation studies performed for (b) (4) and (b) (4) used for mRNA-1273 manufacturing utilized a "Mock" soil process prior to Clean-in-place (CIP) process. However, the "mock" soil process did not simulate the current manufacturing process. The procedure used during cleaning validation studies do not ensure that a similar manufacturing process was followed. For example,

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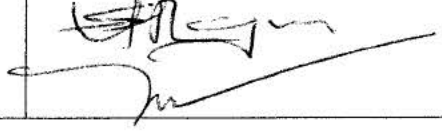
SEE REVERSE OF THIS PAGE		Unnee Ranjan, Lead Investigator Thai D. Truong, Investigator Swati Verma, Product Specialist Ben Firschein, Regulatory Counsel	09/21/2023

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A. During routine manufacturing process, the (b) (4) (b) (4) , Equipment ID# MIX-1805, MIX-1807, MIX-7807, MIX-7805, MIX-3807, and MIX-3805 are utilized for approximately (b) (4) for mixing of (b) (4) batch size of mRNA and lipid nanoparticles. The Cleaning Validation studies (VAL-PRO-6414, approved on 14Dec2022) included a "mock" mixing process of approximately (b) (4) (b) (4) using (b) (4) of drug substance.

B. During routine manufacturing process, the (b) (4) (b) (4) , Equipment ID# MIX-9805 and MIX-8805 are utilized for approximately (b) (4) for mixing of (b) (4) batch size of mRNA and lipid nanoparticles. The Cleaning Validation studies (VAL-PRO-6414, approved on 14Dec2022) included a "mock" mixing process of approximately (b) (4) using (b) (4) of drug substance.

C. During routine manufacturing process, (b) (4) , Equipment ID# CRM-1413 (b) (4) CRM-3413 (b) (4), CRM-7413 (b) (4) and CRM-8413 (b) (4), are utilized for approximately (b) (4) ((b) (4) (b) (4) of approximately (b) (4) using (b) (4)). However, the Cleaning Validation studies included a "mock" process of approximately (b) (4) using (b) (4) product.

OBSERVATION 3

Separate or defined areas to prevent mix-ups are deficient.

Your firm failed to discard or move expired and hold/restricted materials to physical hold location per SOP-0056 "Inventory Management and Control" to prevent the material being used beyond expiration date or restricted date. Expired materials were found utilized beyond their expiration date and restricted materials were utilized in mRNA drug substance production. There are more than two thousand expired items stored in your GMP Warehouse and Cold Storage at time of inspection. These materials are currently stored at the same location with released or in-used materials. There was no clear demarcation between these items in the GMP Warehouse and cold storage.

For example, expired material stored in GMP storage were observed during the walk through on 9/11/2023 and 9/12/2023:

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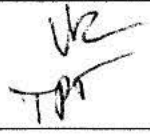
SEE REVERSE OF THIS PAGE		Unnee Ranjan, Lead Investigator Thai D. Truong, Investigator Swati Verma, Product Specialist Ben Firschein, Regulatory Counsel	09/21/2023

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i. (b) (4), Batch# (b) (4), expired 26Aug2023
ii. (b) (4), Batch# (b) (4), expired 27Jul2023.
iii. (b) (4), Batch# (b) (4), expired 19Jul2023.
iv. (b) (4), Batch# (b) (4), expired 17Mar2023.
v. (b) (4), Batch# (b) (4), expired 28Feb2023.
vi. (b) (4), Batch# (b) (4), expired 31Dec2022.

OBSERVATION 4

Written procedures were not followed. Specifically,

A. SOP-0416, Alarm Response Program, required the alarm acknowledgement within (b) (4), impact assessment within (b) (4) of alarm notification and QA review within (b) (4) of impact assessment completion. Your firm failed to respond and follow up on the alarm responses within the timeframe established per SOP-0416. For example:

i. Differential Pressure (DP) alarm for Grade C room 1183 on 6/24/2023 - The alarm acknowledgement and impact assessment were conducted and entered on (b) (4) system during FDA inspection on 9/13/2023.
ii. DP alarm for Grade C room 1183 on 1/30/2023 - The alarm impact assessment was completed on 2/23/2023, QA review was completed on 8/11/2023.
iii. DP alarm for Grade C room 1183 on 1/23/2023 – The alarm impact assessment was completed on 1/23/2023, QA review was completed on 2/8/2023.
iv. Temperature alarm for (b) (4) Cold Storage 1677 on 4/18/2023 – The alarm impact assessment was completed on 4/19/2023, QA review was completed on 7/12/2023.
v. Temperature alarm for (b) (4) freezer 1678 on 1/24/2023 – The alarm impact assessment was completed on 1/24/2023, QA review was completed on 3/16/2023.
vi. Temperature alarm for (b) (4) 1678 on 7/26/2023 – The alarm started on 7/26/2023, alarm acknowledgement on 7/27/2023. There is no impact assessment or QA

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review as of this inspection. The freezer was never taken out of service and currently in used to stored GMP materials.

B. Effectiveness check based on updated cleaning process was not evaluated as per the written program.

Change Control QE-016513 (implementation date of 14Sep2022) was initiated to update the automated cleaning procedure of (b) (4) , Equipment ID# MIX-1805, MIX-1807, MIX-7807, MIX-7805, MIX-3807, and MIX-3805. A cleaning procedure update was implemented based on the change control and a six-month effectiveness check through cleaning verification after each equipment usage (due date: 14Mar2023) was required after the implementation of change actions to review cleaning verification data to ensure automated method change was effective. However, the cleaning verification samples were not collected after 06Feb2023.

OBSERVATION 5

Equipment and Facilities are not designed to minimize potential for contamination.

Specifically, the air handling systems were not adequately designed and controlled to assure appropriate air quality in the Grade C cleanroom in which mRNA drug substance is manufactured. The positive pressure was not consistently maintained between the grade C cleanrooms and grade D Airlocks. Monitoring data from (b) (4) system showed frequent drops of Grade C Cleanroom pressure to negative values between January 2023 and September 2023. The negative DPs (differential pressure) were not assessed for potential impact.

Furthermore, the Cleanroom Open Door recovery study conducted during FDA inspection on 9/15/2023 under VAL-TP-0034 for Grade C room 1311 shows that grade C Cleanroom lost differential pressure to negative value immediately when the door was opened to the Grade D airlock.

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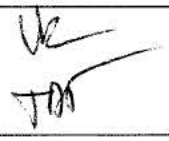
SEE REVERSE OF THIS PAGE		Unnee Ranjan, Lead Investigator Thai D. Truong, Investigator Swati Verma, Product Specialist Ben Firschein, Regulatory Counsel	09/21/2023

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***DATES OF INSPECTION**

9/11/23 (Mon), 9/12/23 (Tue), 9/13/23 (Wed), 9/14/23 (Thu), 9/15/23 (Fri), 9/18/23 (Mon), 9/19/23 (Tue), 9/20/23 (Wed), 9/21/23 (Thu)

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SEE REVERSE OF THIS PAGE		Umee Ranjan, Lead Investigator Thai D. Truong, Investigator Swati Verma, Product Specialist Ben Firschein, Regulatory Counsel	09/21/2023

The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."