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CBER (b) (6) CMC/Facility BLA Review Memorandum

BLA STN 125869/0

Influenza Vaccine, mRNA (mRNA-1010, MFLUSIVA)

(b) (6) Reviewer, (b) (6)

1. **BLA#:** STN 125869/0

2. **APPLICANT NAME AND LICENSE NUMBER:**

ModernaTX, Inc., U.S. License Number 2256

3. **PRODUCT NAME/PRODUCT TYPE**

Influenza Vaccine, mRNA (mRNA-1010, MFLUSIVA)

4. **GENERAL DESCRIPTION OF THE FINAL PRODUCT**

- a. Pharmacological category: mRNA-based vaccine
- b. Dosage form: Injectable suspension
- c. Strength/Potency: 37.5 µg
- d. Route of administration: Intramuscular injection
- e. Indication: Active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B represented in the vaccine for adults 50 years of age and older.

5. **MAJOR MILESTONES**

First committee meeting: December 19, 2025

Filing meeting: January 16, 2026

Filing action: February 17, 2026

Mid-cycle communication: April 6, 2026

Late-cycle communication: June 5, 2026

PDUFA ADD: August 5, 2026

6. (b) (6) **CMC/FACILITY REVIEW TEAM**

Reviewer/Affiliation	Section/Subject Matter
(b) (6)	1 Administrative Information 2.3 Quality Overall Summary 3.2.S Drug Substance 3.2.P Drug Product 3.2.A Appendices 3.2.R Regional Information

7. **SUBMISSIONS REVIEWED**

Date Received	Submission	Comments/Status
December 5, 2025	STN 125869/0	Original submission / Reviewed
March 11, 2026	Amendment STN 125869/0.14 (eCTD 0015)	Response to IR sent on February 24, 2026: confirmed no significant changes to facilities and equipment at approved mRNA manufacturing facilities / Reviewed
June 4, 2026	Amendment STN 125869/0.69 (eCTD 0070)	Response to IR sent on May 22, 2026: (b) (4) manufacturing facility / Reviewed
June 12, 2026	Amendment STN 125869/0.74 (eCTD 0075)	Response to IR sent on June 2, 2026: visual inspection, media fill, shipping validation, (b) (4) validation, container closure integrity testing / Reviewed

Date Received	Submission	Comments/Status
June 26, 2026	Amendment STN 125869/0.84 (eCTD 0085)	Response to IR sent on June 18, 2026: comparability protocols, container closure manufacturers / Reviewed
July 10, 2026	Amendment STN 125869/0.92 (eCTD 0093)	Response to IR sent on July 7, 2026: comparability protocol and (b) (4) facility address / Reviewed

8. REFERENCED REGULATORY SUBMISSIONS

Submission Type & #	Holder	Referenced Item	Letter of Cross-Reference	Comments/Status
BL 125835	ModernaTx, Inc.	Entire BLA	Yes	MNEXSPIKE (COVID-19 Vaccine)
BL 125796	ModernaTx, Inc.	Entire BLA	Yes	MRESVIA (Respiratory Syncytial Virus Vaccine)
BL 125752	ModernaTx, Inc.	Entire BLA	Yes	SPIKEVAX (COVID-19 Vaccine, mRNA)
DMF (b) (4)	(b) (4)	(b) (4)	Yes	No DMF review required. Information pertinent to container closure is provided in the BLA.
DMF (b) (4)	(b) (4)	(b) (4) syringe	Yes	No DMF review required. Information pertinent to container closure is provided in the BLA.
DMF (b) (4)	(b) (4)	Elastomeric formulation, coatings and films (plunger)	Yes	No DMF review required. Information pertinent to container closure is provided in the BLA.

9. ACRONYM KEY

Abbreviations/Acronyms	Description
DP	Drug product
DS	Drug substance
DSPC	Lipid component (1,2-distearoyl-sn-glycero-3-phosphocholine)
LDP	Labeled drug product

Abbreviations/Acronyms	Description
(b) (4)	(b) (4)
LNP	Lipid nanoparticle
LNP-(b) (4) LNP-(b) (4) LNP-(b) (4)	Lipid nanoparticles used in mRNA-1010 seasonal influenza vaccine LNP drug substance
mRNA	Messenger ribonucleic acid
PEG2000-DMG	Lipid component (1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000)
PFS	Prefilled syringe
RNA	Ribonucleic acid
RNA-(b) (4) RNA-(b) (4) RNA-(b) (4)	Ribonucleic acid used in the mRNA-1010 vaccine.
SM-102	Lipid component (heptadecan-9-yl 8-((2-hydroxyethyl)(6-oxo-6-(undecyloxy)hexyl)amino)octanoate)
UDP	Unlabeled drug product

Reference is made to the original Biologics License Applications (BLA) and BLA supplements listed in the table below for approved mRNA vaccines. This review memo leverages previously reviewed and approved information that is the same information relevant to mRNA-1010. The approved vaccines are referenced in the DS, DP, facilities and equipment appendices, and regional information sections of this review memo according to the chemical or proprietary names (i.e., mRNA-1273 or SPIKEVAX) hereinafter. All references to previously approved BLA supplements for ModernaTX Inc.'s mRNA vaccines are identified as such and are documented in the applicable sections in this review memo. All other references are to the original BLAs hereinafter (i.e. previously reviewed for mRNA-1273).

ModernaTX, Inc.'s FDA Approved mRNA Vaccines - Original BLAs and BLA Supplements

BLA STN	Established and (Proprietary) Name	Chemical Name	Contents Applicable to mRNA-1010 Manufacturing	Approval Date
125752/0	COVID-19 Vaccine (SPIKEVAX)	mRNA-1273	Original BLA	January 31, 2022
125752/74	COVID-19 Vaccine (SPIKEVAX)	mRNA-1273	Introduction of PFS presentation	September 11, 2023
125752/90	COVID-19 Vaccine (SPIKEVAX)	mRNA-1273	Introduction of (b) (4) fill line (b) (4) facility	September 28, 2023
125752/208	COVID-19 Vaccine (SPIKEVAX)	mRNA-1273	(b) (4) facility and equipment	August 9, 2024
125796/0	RSV Vaccine (MRESVIA)	mRNA-1345	Original BLA	May 31, 2024
125835/0	COVID-19 Vaccine (MNEXSPIKE)	mRNA-1283	Original BLA	May 30, 2025

COVID-19: coronavirus disease of 2019; Food and Drug Administration; RSV: respiratory syncytial virus

10. REVIEWER SUMMARY AND RECOMMENDATION

A. EXECUTIVE SUMMARY

ModernaTX, Inc. (Moderna hereinafter) submitted BLA 125869/0 for Influenza Vaccine, mRNA (MFLUSIVA) (mRNA-1010 hereinafter), an LNP-encapsulated trivalent influenza (TIV) mRNA-based vaccine indicated for active immunization for the prevention of influenza disease. The applicant is seeking traditional approval for adults 50 through 64 years of age and accelerated approval for adults 65 years of age and older. This submission was granted priority review with an 8-month review cycle.

The mRNA-1010 vaccine encodes the full-length, membrane-bound influenza hemagglutinin (HA) glycoproteins of the three seasonal influenza strains recommended annually by the World Health Organization (WHO) for cell or recombinant-based vaccines: A/H1N1, A/H3N2, and B/Victoria-lineage. The SM-102-based LNP technology for mRNA-1010 is the same proprietary LNP system used in Moderna's mRNA vaccines, including mRNA-1273 (SPIKEVAX), mRNA-1345 (MRESVIA), and mRNA-1283 (MNEXSPIKE), all currently licensed in the United States (US).

This (b) (6) review memo includes summaries and assessments of the DS and DP manufacturing processes, microbial quality attributes, facility information including utilities, contamination/cross-contamination controls, qualifications and maintenance of classified environments and manufacturing equipment, and cleaning and sterilization processes.

The pre-license inspections (PLIs) for the DS and DP manufacturing facilities (b) (4) were waived based on each facility's inspection history and compliance status. The basis for waiving the PLIs of these facilities is documented in a separate inspection waiver memo uploaded in CBER Connect under BLA STN 125869.

B. RECOMMENDATION

I. APPROVAL

Approval of BLA 125869/0 is recommended based on the review of the information submitted to the original BLA and corresponding amendments, and in conjunction with the inspectional compliance history evaluations, the production process, facilities, equipment, and controls appear acceptable for the licensure of mRNA-1010.

The mRNA-1010 DS and DP manufacturing facilities to be named in the approval letter are listed below. Refer to common technical document (CTD) section 3.2.A *Appendices* of this review memo for a complete list of DS and DP manufacturing and testing facilities.

- (b) (4)

(b) (4)

- ModernaTX, Inc. (DS manufacturing)

(b) (4)

- (b) (4) (DP manufacturing)
(b) (4)

(b) (4)

- (b) (4) (DP primary labeling and packaging)

(b) (4)

- (b) (4)

The following comparability protocols (CP) are recommended for approval:

1. Implementation of ModernaTX (b) (4) as an alternative manufacturer for mRNA-1010 (b) (4). The data will be provided in a Prior Approval Supplement (PAS).
2. Introduction of annual seasonal strain(s) update for mRNA-1010. The data will be provided in a PAS.

Approval is recommended with the following inspectional recommendation at the (b) (4)

CBER understands that the recommendation may or may not be taken (based on risk and available resources) and is not requesting documentation to be submitted as evidence of completion.

- Evaluate the final shipping validation at 2°C to 8°C using active shippers and temperature-controlled vehicle shipping systems

II. SIGNATURE BLOCK

Reviewer/Title/Affiliation	Concurrence	Signature and Date
(b) (6)	Concur	
(b) (6)	Concur	
(b) (6)	Concur	

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Module 3

3.2.S DRUG SUBSTANCE

The mRNA-1010 DS is comprised of (b) (4), each consisting of one RNA encapsulated in (b) (4) and (b) (4). (b) (4) is comprised of SM-102, PEG2000-DMG, DSPC, and cholesterol. The (b) (4) is the starting material for RNA.

RNA-LNP Components

RNA	LNP
(b) (4) encodes the glycoprotein HA of the seasonal influenza A/Massachusetts/18/2022 (A/H3N2)-like- virus.	LNP-(b) (4)
(b) (4) encodes the glycoprotein HA of the seasonal influenza B/Austria/1359417/2021 (B/Victoria lineage) virus.	LNP-(b) (4)
R(b) (4) encodes the glycoprotein HA of the seasonal influenza A/Wisconsin/67/2022 (A/H1N1) virus.	LNP-(b) (4) 1

The LNP DS is (b) (4) materials.
The (b) (4) are stored at (b) (4) prior to further manufacturing into the DP.

3.2.S.2 Manufacture

3.2.S.2.1 Manufacturer(s)

See section 3.2.A *Appendices* for a complete list of DS manufacturing and testing facilities.

3.2.S.2.2 Description of Manufacturing Process

(b) (4)

[REDACTED]

16 pages determined to be not releasable: (b)(4)

(b) (4)



3.2.P DRUG PRODUCT

3.2.P.1 Description and Composition of the Drug Product

The mRNA-1010 DP is an RNA-lipid complex dispersion that contains three monovalent LNPs. The RNA in each monovalent LNP encodes for the following proteins:

- Influenza A/H1N1 (b) (4)
- Influenza A/H3N2 (b) (4)
- Influenza B/Victoria (b) (4)

The LNP consists of four lipids (SM-102, cholesterol, DSPC, and PEG2000-DMG) that act as protectants and carriers of the RNA. The DP is supplied as a sterile, single dose,

ready-to-use (RTU) liquid for intramuscular administration at a 37.5 µg dose at 0.10 mg/mL. The combination product consists of the mRNA-1010 DP filled in a CCS consisting of a 1-mL PFS with a plunger rod and plunger. Each PFS delivers 12.5 µg of RNA and 759 µg of total lipids as a white to off-white dispersion in preservative-free buffer.

3.2.P.2.5 Microbiological Attributes

Microbiological attributes of the DP are controlled through the manufacturing process, release and stability testing, container closure suitability, and environmental controls. The DP is manufactured by a conventional aseptic process using (b) (4) bioburden is monitored during the manufacturing process, and (b) (4) is tested (b) (4) (refer to section 3.2.P.3.4 *Controls of Critical Steps and Intermediates*). Microbiological testing is performed for sterility and bacterial endotoxins at release (refer to section 3.2.P.5.1 *Specifications*). The microbiological suitability of the primary CCS was demonstrated through container closure integrity (CCI) and (b) (4) testing (refer to section 3.2.P.7 *Container Closure System*). CCI is monitored as part of the manufacturing process and annually as part of the stability testing program. Maintenance of the aseptic manufacturing environment at the UDP manufacturing facility, (b) (4), is assured through facility controls (refer to section 3.2.A.1 *Appendices – (b) (4)*

3.2.P.3 Manufacture

3.2.P.3.1 Manufacturer(s)

Refer to section 3.2.A *Appendices* for a complete list of all DP manufacturing and testing facilities.

3.2.P.3.3 Description of Manufacturing Process

The mRNA-1010 DP is manufactured at (b) (4)

The mRNA-1010 DP is manufactured at (b) (4)

(b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

After assembly, labeling, and packaging, units are collected for LDP product quality release testing.

The DP is shipped domestically and internationally to third-party logistics partners for commercial distribution (refer to the facilities table in section 3.2.A *Appendices* for storage and distribution locations). Shipments are performed by (b) (4) transportation using qualified passive shippers or temperature-controlled vehicles to maintain the defined shipping temperature (refer to section 3.2.P.3.5 *Process Validation and/or Evaluation – Shipping Validation*).

The microbial-related IPCs, CIPCs and process parameters for the mRNA-1010 DP manufacturing process are described in section 3.2.P.3.4 *Controls of Critical Steps and Intermediates* of this review memo.

Reviewer's comment: The description of the mRNA-1010 DP manufacturing process was reviewed and appears acceptable. The manufacturing steps that are critical to microbial quality, including (b) (4), filling, and plunger placement are included in the process.

3.2.P.3.4 Controls of Critical Steps and Intermediates

The microbial control/sterility assurance-related IPCs and CIPCs are listed in the table below. The IPCs identified as CIPCs are annotated.

mRNA-1010 DP Production IPCs		
Process Step	Test	Acceptance Criteria
(b) (4)	(b) (4)	(b) (4)
(b) (4)	(b) (4)	(b) (4)
(b) (4)	(b) (4)	(b) (4)
(b) (4)	(b) (4)	(b) (4)
(b) (4)	(b) (4)	(b) (4)
Filling	(b) (4)	(b) (4)
Filling	(b) (4)	(b) (4)
Filling	Container closure integrity (b) (4) method)	(b) (4)

1. Tests identified as CIPCs.

(b) (4)

Process parameters for (b) (4), aseptic filling, and plunger placement are listed in the table below.

(b) (4)

The firm indicates that the DP manufacturing process is intended to be performed (b) (4)

The process is completed in a specified cumulative process duration (b) (4) with a specified maximum duration for time out of refrigeration (b) (4)

(b) (4)

Reviewer's comment: The microbial control/sterility assurance-related IPCs, CIPCs, and process parameters were reviewed and appear acceptable. The manufacturing steps that are critical to microbial quality, including (b) (4), filling, and plunger placement are included in the process. The PFS fill and finish manufacturing process appears to have an acceptable control strategy to assure product quality and process consistency for sterility assurance. Refer to section 3.2.P.3.5 Process Validation and/or Evaluation – Process Performance Qualification for the (b) (4) hold time study. Assessment of all other IPCs, CPPs and process parameters from a DP quality perspective not germane to microbial control or sterility assurance is deferred to the OVRR reviewer.

3.2.P.3.5 Process Validation and/or Evaluation

Process Performance Qualification

A PPQ was conducted for the mRNA-1010 (RNA-101) TIV FLU Vaccine commercial manufacturing process at (b) (4)



mRNA-1010 PPQ Lots Executed for the DP Manufacturing Process

UDP Lot (CMO Lot)	UDP DOM	Theoretical Units	LDP Lot (CMO Lot)	LDP DOM
(b) (4)				

1. Manufactured according to Process (b) (4)
2. Manufactured according to Process (b) (4)

mRNA-1010 PPQ Lots - Filling and Plunger Placement Process

PPQ Lot	Total Units Filled	Accepted Units	Rejected Units ¹	Filling Yield (%)
(b) (4)				

1. Corridor rejections refer to fallen units or non-compliant IPCs after exiting the filling line.

All IPCs, CIPCs, and process parameters for (b) (4), aseptic filling, plunger placement noted in section 3.2.P.3.4 *Controls of Critical Steps and Intermediates* met the acceptance criteria. All release acceptance criteria noted in section 3.2.P.5 *Control of Drug Product* were met.

The following hold times were challenged during PPQ:

- (b) (4)

test results met the acceptance criteria.

- (b) (4)

All results met the acceptance criteria.

One major deviation occurred that impacted PPQ batches (b) (4)

An impact assessment was conducted, and the firm concluded that there was no impact on product quality or the PPQ. All CPPs, environmental controls, and microbiological results met the acceptance criteria. The deviation was resolved and closed.

Reviewer's comment: *The PPQ for the mRNA-1010 DP manufacturing process was reviewed and appears acceptable. All microbial control/sterility assurance-related IPCs, CIPCs, process parameters and release results met the acceptance criteria. The manufacturing process is considered validated. Microbial testing conducted during the hold time studies appear to confirm that the manufacturing procedures and controls are acceptable to meet the microbial control requirements for the (b) (4) and filling process. The cumulative process duration and (b) (4) were assessed; however, no microbial testing was performed. Therefore, review is deferred to the OVRR reviewer.*

Visual Inspection and AQL

100% automated visual inspection (AVI) for the three PPQ lots was conducted at (b) (4) using the (b) (4). The AVI results are listed in the table below.

mRNA-1010 PPQ - AVI						
PPQ Lot	Inspected Units	Accepted Units	Rejected Units	Rejected in AQL	Sampled Units	Yield (%)
(b) (4)						

The number of units rejected prior to AVI and broken during inspection are provided in the submission.

After visual inspection, an AQL sample set is manually inspected following the criteria set in (b) (4) with a general inspection level and rigorous inspection type III. The acceptance criteria for AQL and a full listing of critical, major, and minor defects were provided in amendment STN 125869/0.74 (eCTD 0075). The AQL acceptance criteria for critical defects (i.e., (b) (4)), major defects (i.e., (b) (4)), and minor defects (i.e., (b) (4)) are listed in the table below.

AQL Acceptance Criteria			
Defect Severity	AQL Acceptance Criteria	Limits of Accepted Units	Limits of Rejected Units
Critical	(b) (4)		
Major			
Minor			

All AQL acceptance criteria were met.

Reviewer's comment: The AVI and AQL results were reviewed and appear acceptable. Visual inspection of mRNA-1273, mRNA-1283, and mRNA-1010 DP PFS is performed on the (b) (4). The (b) (4) was first approved for the visual inspection of mRNA-1273 PFS in BLA supplement STN 125752/90. The qualification was verified for ModernaTX's most recently approved vaccine, mRNA-1283 PFS, in BL STN 125835/0.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Aseptic Process Simulation (APS)

An APS (media fill studies) was conducted at (b) (4) simulating the DP aseptic process using the commercial equipment, parameters, and materials to test maximum hold times, simulate process interventions (including personnel shift change), and confirm that a minimum number of filled syringes are negative for microbial growth. Initial media fill studies were conducted with (b) (4) batches ((b) (4) (b) (4)) to validate aseptic filling operations on the (b) (4) filling line for DP filling in the 1-mL long COC PFS.

(b) (4)

(b) (4)



Shipping Validation

(b) (4)



(b) (4)

3.2.P.5 Control of Drug Product

3.2.P.5.1 and 3.2.P.5.6 Specification(s) and Justification of Specification(s)

The mRNA-1010 DP release specifications the following in the table.

mRNA-1010 DP Release Specifications

Attribute (b) (4)	Analytical Procedure	Release Specification	Stability Shelf-Life Acceptance Criteria
Bacterial Endotoxin (b) (4)	(b) (4)	(b) (4)	(b) (4)
Sterility (b) (4)	(b) (4)	No Growth	No Growth
Deliverable Volume (b) (4)	(b) (4)	(b) (4)	(b) (4)
(b) (4)	(b) (4)	(b) (4)	(b) (4)
(b) (4)	(b) (4)	(b) (4)	(b) (4)
Container Closure Integrity (b) (4)	(b) (4)	N/A	Pass

(b) (4)

Container closure integrity is performed to confirm maintenance of sterility during stability. CCIT is performed only on stability in lieu of sterility.

Reviewer's comment: *The mRNA-1010 DP release specifications associated with microbial quality were reviewed and appears acceptable. The assessment of all the other release tests is deferred to OVRR reviewer.*

3.2.P.5.2 and 3.2.P.5.3 Analytical Procedures and Validation of Analytical Procedures

Refer to section 3.2.P.7 *Container Closure System* for an assessment of CCIT.

3.2.P.5.4 Batch Analyses

The three mRNA-1010 PPQ lots manufactured from (b) (4), for PPQ-comparability and stability studies are listed in the PPQ section of this review memo in section 3.2.P.3.5 *Process Validation and/or Evaluation - PPQ*. The acceptance criteria for the mRNA-1010 UDP and corresponding LDP PPQ lots are listed in section 3.2.P.5.1 and 3.2.P.5.6 *Specification(s) and Justification of Specification(s)*. All results met the acceptance criteria for bacterial endotoxins, sterility, deliverable volume, (b) (4) specifications.

Reviewer's comment: Batch release testing results associated with sterility assurance were reviewed and appear acceptable.

3.2.P.7 Container Closure System

The mRNA-1010 DP is supplied as a sterile, single-dose, RTU dispersion in a PFS. The primary CCS consists of a 1-mL long syringe, 1-mL long plunger, and a plunger rod. The syringe and plunger are supplied sterile and RTU. The syringes are received in plastic tubs with polypropylene nests and (b) (4) lids. The plunger rod is supplied non-sterile and RTU. The syringe and plunger are compliant with (b) (4) requirements. The (b) (4) standards are listed in the table below.

mRNA-1010 DP Primary Container Closure Components

Component	Description	Manufacturer	Sterility Control	Standards
Syringe	1-mL long COC with halobutyl rubber tip cap in rigid plastic cover	(b) (4)	(b) (4)	
Plunger	1-mL long halobutyl rubber plunger with fluoropolymer coating on product contact surface			
Plunger Rod	Polypropylene plunger rod		N/A	N/A

COC = cyclic olefin copolymer; SAL= Sterility Assurance Level

The secondary packaging for the mRNA-1010 DP is an assembled and labeled PFS packed into a carton and placed into a case with one patient information leaflet or prescribing information.

In amendment STN 125869/0.74 (eCTD 0075), ModernaTX confirmed that the primary CCS used for mRNA-1010 DP PFS is the same as that used for previously approved

mRNA vaccines: mRNA-1273, mRNA-1345, and mRNA-1283. No CCS specification changes, including changes to quality control inspection methods, manufacturers, or suppliers, have been made since the Agency's approval of ModernaTX's mRNA products.

Container Closure Integrity Test (CCIT)

The intended manufacturing, storage, and use conditions for the mRNA-1010 DP include (b) (4) temperatures for both the UDP (no plunger rod) and LDP (plunger rod assembled).

In amendment STN 125869/0.74 (eCTD 0075), ModernaTX confirmed that the validated (b) (4) CCIT method used for ModernaTX's previously approved mRNA vaccines is applicable to the mRNA-1010 PFS DP CCS. The CCI validation of the limit of detection is as follows:

- Positive control: (b) (4)

- Negative control: (b) (4)

Method verification is performed for subsequent products within the same product family with differences in fill volume.

CCI of the mRNA-1010 UDP was verified for the three commercial scale PPQ batches (b) (4). PFS were manufactured at the target plunger insertion parameters. For each PPQ lot, a total of (b) (4) PFS units were assessed for CCI using the validated (b) (4) method. (b) (4) were collected following visual inspection. All results met the acceptance criteria (b) (4) not detected).

CCI of mRNA-1010 LDP through the end of shelf-life are verified as part of ongoing stability testing. CCI of LDP at (b) (4) after accelerated aging (b) (4) and after transit simulation (b) (4) are verified as part of design verification testing. CCI was tested on the samples according to the (b) (4) method. All results met the acceptance criteria ((b) (4)).

Functionality tests were performed for the CCS. The testing includes (b) (4), and deliverable volume. Design verification data demonstrates the suitable functionality of the 1-mL long plunger as a closure for the 1-mL long COC syringe in conjunction with the 1-mL long plunger rod. Design verification is assessed in Section 3.2.R *Regional Information (USA) – Combination Products* in this review memo.

A method verification was conducted for (b) (4) in the PFS with a plunger stopper, plunger rod, and 1.5" 27-gauge needle. A total of (b) (4) samples were tested for (b) (4) by (b) (4) operators (b) (4) samples per operator). All results met the acceptance criteria. No deviations were noted.

Reviewer's comment: *The description of the CCS appears acceptable. The same syringe components for mRNA-1010 PFS DP are used for mRNA-1273, mRNA-1345, and mRNA-1283 vaccines. The descriptions, microbial specifications (endotoxin and sterility), technical specifications, and drawings and dimensions applicable to the mRNA-1010 DP primary CCS were previously reviewed in BL 125796/0 (MRESVIA) and were found acceptable. A method verification was performed for the mRNA-1010 PFS configuration demonstrating that the validated (b) (4) method remains suitable for assessing CCI of the mRNA-1010 PFS CCS.*

Plunger Placement

Plunger movement testing was performed on the primary CCS to demonstrate that migration of the plunger in the syringe barrel does not exceed the sterile barrier length during storage and transportation conditions. Testing simulated expected worst-case storage and transportation conditions for both UDP and LDP. The simulation consisted of UDP (b) (4)

To assess worst-case combinations of (b) (4), PFS were tested under (b) (4) conditions, covering the IPC limits for fill volume and plunger insertion depth. The targeted plunger position control limit for (b) (4) of fill volume is (b) (4) of plunger depth.

(b) (4)

(b) (4)

The results indicate that the plunger movement is smaller than the length of the sterile barrier (b) (4).

Reviewer's comment: *The plunger movement test results appear to support the established plunger position control strategy which minimizes the risk of plunger movement. The plunger position control limits of the PFS (b) (4) of plunger insertion depth) appear to be acceptable to*

maintain the plunger movement within the length of the sterile barrier of the CCS under worst-case storage and transportation conditions.

3.2.P.8 Stability

3.2.P.8.1 Stability Summary and Conclusion and 3.2.P.8.3 Stability Data

The proposed shelf-life for mRNA-1010 DP in the commercial primary CCS is up to 12 months at 2°C to 8°C refrigerated storage, including up to 12 hours at 8°C to 25°C at the point-of-care site. The three mRNA-1010 PPQ lots (b) (4) were placed on long-term stability for up to 12 months at (b) (4) 2°C to 8°C, and on accelerated stability for (b) (4). In general, the lots are tested for endotoxins (b) (4) CCI by (b) (4) (pass), sterility (no growth), deliverable volume (b) (4) 0.38 mL, and (b) (4) at the following time intervals. A full list of time intervals is provided in the submission

- (b) (4)
- 2°C to 8°C: 0-, 1-, 3-, 6-, 9- and 12-months
- (b) (4)

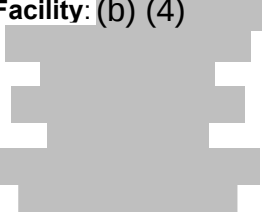
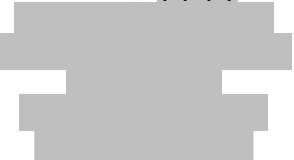
Stability studies are ongoing with up to three months of data available for the PPQ lots.

Reviewer's comment: *The available stability data was reviewed and appears acceptable. Microbial stability data beyond three months are not yet available; therefore, no additional data is available to assess the shelf-life expiry. This appears to be low-risk as the mRNA-1010 DP uses the same primary CCS (but with varying plunger insertion depths) as the approved mRNA-1345 and mRNA-1283 vaccines, in which stability has been demonstrated. The varying plunger position is low-risk because the stopper remains within the sealed region of the syringe barrel and the radial compression of the stopper against the barrel wall is maintained. The review of all other product-specific stability data is deferred to the OVRP reviewer.*

3.2.A APPENDICES

FACILITIES TABLE

Facility Manufacturing/ Testing activities	Inspection? Waiver? Not required?	Compliance check required for approval?	RMS-BLA entry required?	CMO	Comments
Facility: (b) (4) Manufacturing and release testing of (b) (4)	Waiver	Yes	Yes	Yes	(b) (6) (b) (4) NAI
Facility: ModernaTX, Inc. (b) (4) Manufacturing of (b) (4) DS Intermediates; In-process, release, and stability testing of (b) (4) In-process and release, testing of (b) (4) ; Storage of (b) (4) and LNP DS	Waiver	Yes	Yes	No	(b) (6) (b) (4) NAI
Facility: (b) (4) Manufacturing of UDP In-process testing of DP	Waiver	Yes	Yes	Yes	(b) (6) (b) (4) VAI

Facility Manufacturing/ Testing activities	Inspection? Waiver? Not required?	Compliance check required for approval?	RMS-BLA entry required?	CMO	Comments
Facility: (b) (4)  Storage of (b) (4)	Not Required	No	Yes	Yes	N/A
Facility: (b) (4)  Storage of RNA DS Intermediate and LNP DS	Not Required	No	Yes	Yes	N/A
Facility: (b) (4)  Storage of RNA DS Intermediate and LNP DS	Not Required	No	Yes	Yes	N/A
Facility: (b) (4)  Release testing of (b) (4) DS intermediate; In-process, release and stability testing of LNP DS	Not Required	No	Yes	Yes	N/A
Facility: (b) (4)  Release testing of (b) (4) DS Intermediate	Not Required	No	Yes	Yes	N/A

Facility Manufacturing/ Testing activities	Inspection? Waiver? Not required?	Compliance check required for approval?	RMS-BLA entry required?	CMO	Comments
Facility: (b) (4)  Storage of LNP DS	Not Required	No	Yes	Yes	No FEI
Facility: (b) (4)  DP distribution	Not Required	No	No	Yes	N/A
Facility: (b) (4)  DP distribution	Not Required	No	No	Yes	N/A

(b) (4)
; CDER: Center for Drugs Evaluation and Research; (b) (6)
DP: drug product; DS: drug substance; LDP: labeled drug product; (b) (4)
; LNP: lipid nanoparticle; (b) (4)
MRA: Mutual Recognition Agreement; N/A: not applicable; NAI:
no action indicated; (b) (6)
; RNA: ribonucleic acid; UDP: unlabeled drug product; VAI: voluntary action indicated; (b) (4)

(b) (4)



(b) (4)

ModernaTX, Inc. (DS Intermediates and DS)

The (b) (4) at ModernaTX is a multi-product manufacturing and testing facility for clinical and commercial mRNA-based products. ModernaTX is currently approved to manufacture the DS for mRNA-1273, mRNA-1345, and mRNA-1283. The facility also manufactures the (b) (4) building.

Commercial Manufacturing Areas at ModernaTX (b) (4) for mRNA-1010

Manufacturing Process	Room	Process Train	Room Classification
RNA DS Intermediate	(b) (4)	(b) (4)	(b) (4)
(b) (4) Intermediate			
LNP DS			
(b) (4)		N/A	
(b) (4)		N/A	

ModernaTX provided details regarding all major changes that occurred at the ModernaTX facility since the approval of ModernaTX's most recent mRNA vaccine, mRNA-1283, that are applicable to the manufacture of mRNA-1010 DS Intermediates and DS in amendment STN 125869/0.14 (eCTD 0015). The firm indicated that one major facility/utility change occurred. According to a change control implemented June 24, 2025, ModernaTX upgraded designated spaces in Building (b) (4) from controlled non-classified (CNC) to Grade (b) (4) classifications to meet regulatory requirements, enhance contamination control, and support process and product quality. The change control was limited to the hallways and airlocks and did not include any of the manufacturing suites. The firm indicated in amendment STN 125869/0.85 (eCTD 0085) that the change was provided in an annual report (BLA 125752/368 (eCTD 0539)).

Reviewer's comment: Since the approval of ModernaTX's most recent mRNA vaccine, mRNA-1283, the CNC hallways and airlocks were upgraded to a Grade (b) (4) classification. This upgrade improves contamination controls and appears to pose no risk to the mRNA-1010 DS manufacturing process in the Grade (b) (4) areas. The annual report status with the Agency for the classification upgrade is still under "performing initial review." No other major changes were made to facility design and facility flows, HVAC systems and EM, critical product contact utilities,

contamination/cross-contamination controls (facility cleaning, disinfectant effectiveness, changeover/line clearance), and computerized systems. The firm provided summaries of these facility aspects in amendment STN 125869/0.14 (eCTD 0015). The information was reviewed and appears acceptable.

The facility areas used to manufacture mRNA-1010 DS are identical to the areas used to manufacture mRNA-1283 DS. The mRNA-1010 DS is manufactured in the same areas as mRNA-1345; however, the mRNA-1345 DS manufacturing process also uses additional areas (RNA manufacturing rooms (b) (4) manufacturing rooms (b) (4) that are not used for mRNA-1010. The ModernaTX facility for mRNA-1010 DS manufacturing leverages the review of BL STN 125835/0 and BL STN 125796/0.

Equipment

ModernaTX provided a list of process equipment used for the manufacture of mRNA-1010 as compared to previously approved vaccines, mRNA-1345 and mRNA-1283, in amendment STN 125869/0.14 (eCTD 0015). ModernaTX indicated that the equipment used across products is identical within each manufacturing product train. Manufacturing is campaign-based. There are no product-specific equipment modifications unique to mRNA-1010 with respect to mRNA-1345 or mRNA-1283. Equipment utilized for mRNA-1010 DS is not product-dedicated and is operated under established multi-product controls and validated changeover procedures consistent with previously approved products.

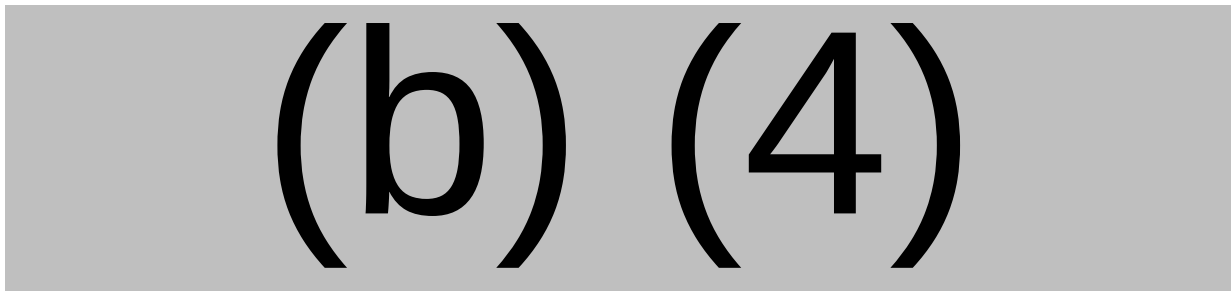
Reviewer's comment: *The firm provided summaries of equipment qualifications and a list of major process equipment used for the manufacture of mRNA-1010 as compared to previously approved vaccines, mRNA-1345 and mRNA-1283 in amendment STN 125869/0.14 (eCTD 0015). The amendment was reviewed and appears acceptable. No major changes were made to major equipment qualifications or equipment cleaning.*

The process train equipment used to manufacture mRNA-1010 DS is identical to the equipment used to manufacture mRNA-1283 DS. The mRNA-1010 DS is manufactured with the same process train equipment as mRNA-1345; however, the mRNA-1345 DS manufacturing process also uses additional equipment in areas that are not used for mRNA-1010.

The DS manufacturing areas and process train equipment were previously reviewed under BL 125796/0 and were found acceptable. The addition of Grade (b) (4) room (b) (4) was previously reviewed under BL 125835/0 and was found acceptable. Therefore, the equipment used for mRNA-1010 DS manufacturing in (b) (4) at the ModernaTX facility leverages the review of BL 125835/0 and BL 125796/0.

(b) (4)

(b) (4)



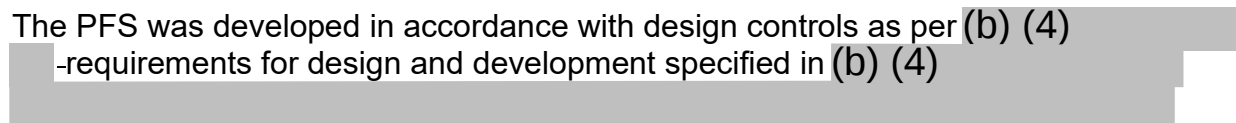
(b) (4)



3.2.R Regional Information (USA)

Combination Products

The PFS was developed in accordance with design controls as per (b) (4)
-requirements for design and development specified in (b) (4)



Design verification demonstrated functional performance according to the applicable (b) (4) standards. Design verification (i.e., (b) (4), deliverable volume) for mRNA-1010 (0.38 mL) PFS includes data from the approved mRNA-1273 PFS presentations (0.5 mL and 0.25 mL). mRNA-1010 and mRNA-1273 PFS use the

same syringe barrel and plunger components, with identical fixed internal dimensions. The only difference between the presentations is the fill volume and resulting plunger position. Since the syringe barrel geometry, stopper interface, physical and chemical DP properties, headspace, and manufacturing processes are similar, the plunger travel and residual “dead” volume that govern dose delivery are independent of fill volume. Therefore, data generated from mRNA-1273 PFS is representative of mRNA-1010 product performance.

A summary of the design verification acceptance criteria and results for mRNA-1010 PFS and representative product, mRNA-1273 PFS, is provided in the original submission in section 3.2.R *Regional Information {Prefilled Syringe Combination}*. Testing was conducted on components at time points T=0, post simulated transportation at 2°C to 8°C and (b) (4). All results met the acceptance criteria for (b) (4), deliverable volume, (b) (4), CCI (b) (4) by (b) (4), and product label visual inspection.

Reviewer’s comment: Design verification data for the mRNA-1010 PFS was reviewed and appears acceptable. ModernaTX confirmed that the primary CCS components for mRNA-1010 PFS DP are the same as the components approved for ModernaTX’s mRNA vaccines mRNA-1273 (STN 125752/74), mRNA-1345, and mRNA-1283. Therefore, review of the remaining design controls (i.e., design history, inputs and outputs, etc.) and other following critical aspects for the manufacture of the device constituent of the combination product leverages the review in STN 125752/74, STN 125796/0, and 125835/0:

- (b) (4) - Management responsibility
- (b) (4) - Purchasing controls
- (b) (4) - Corrective and preventive actions
- Risk analysis (leveraged from 125752/74 and STN 125796/0)

Comparability Protocols

ModernaTX submitted two comparability protocols (CP) containing information under (b) (6) purview:

1.) Implementation of ModernaTX as an alternate manufacturer for mRNA-1010 (b) (4)

2.) Introduction of an annual seasonal influenza strain(s) update for mRNA-1010

(b) (4)

