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(b) (6) ANALYTICAL METHOD REVIEW MEMO

To: 125869/0

From: (b) (6)

Through: (b) (6)

Product: MFLUSIVA (mRNA-1010) influenza vaccine, mRNA

Sponsor: ModernaTX, Inc.

Subject: Review of analytical chemistry methods for the lot release of MFLUSIVA (mRNA-1010)

Recommendation: Approval

Executive Summary

The following analytical chemistry methods were reviewed across multiple manufacturing sites:

1. (b) (4) Methods (Appearance, Deliverable Volume, (b) (4))
2. (b) (4)
3. (b) (4)
4. Total RNA by (b) (4)
5. Total RNA by (b) (4) (DP)
6. (b) (4) (DP)
7. Lipid Identity, Content, and Impurities by (b) (4), (DP)
8. (b) (4)
9. (b) (4)
10. mRNA Purity by (b) (4) (DP)
11. Identity (b) (4) (DP)

Conclusion

The analytical chemistry lot release methods and qualifications for MFLUSIVA (b) (4) drug product (DP) were reviewed and found to be adequate for their intended use.

The (b) (4) site was validated for (b) (4) method as a limit test but later converted to a quantitative test without additional validation. The sponsor has committed to submitting additional supplemental validation of (b) (4) by (b) (4), and additional intermediate precision and linearity results for mRNA purity of DP for Moderna (b) (4) and Moderna (b) (4).

Background

On December 05, 2025, ModernaTX, Inc. submitted Biologics License Application (BLA) 125869/0 for MFLUSIVA (mRNA-1010).

MFLUSIVA is a trivalent mRNA vaccine indicated for active immunization of persons 50 years of age and older against influenza. It is a suspension for intramuscular injection in a pre-filled syringe, stored at 2–8 °C.

Materials

The product is derived from the following materials:

- **RNA** (critical components): Monovalent mRNA solutions, updated seasonally, each encoding the hemagglutinin (HA) glycoprotein of a different influenza strain.
- (b) (4)
- **DS**: Three monovalent RNA-LNP solutions, each formed by (b) (4) into LNPs (b) (4).
- **DP**: Three DS solutions (b) (4) formulated and filled into the final container.

Sites

The following sites are used in lot release testing, validation, or batch analysis (specific testing sites to be listed in the review narrative below):

- (b) (4)
- **Moderna** (b) (4) : ModernaTX, Inc., (b) (4)
- **Moderna** (b) (4) : Moderna (b) (4)
- **Moderna** (b) (4) : ModernaTX, Inc., (b) (4)
- (b) (4)
- (b) (4)
- (b) (4)

(b) (4)

Product Formulations and Component Nomenclature

This BLA includes data for multiple seasonal DP formulations. The original submission presented the (b) (4) formulation, and Amendment 18 began the Annual Strain Update for (b) (4); in this memo, validations for both (b) (4) are reviewed. The formulations and their constituent RNA sequences are defined below.

Table 1. mRNA-1010 Product Formulations

Season*	Formulation	Component RNA Sequences
Development only	(b) (4)	
SH 2022		
2023/2024		
2023/2024		
2024/2025		

Season*	Formulation	Component RNA Sequences
2026/2027		(b) (4)

* Seasons for Northern Hemisphere (NH) unless otherwise noted

† Denotes the formulations presented in Module 3 of this BLA.

(b) (4)

Platform Methods

The sponsor utilizes platform methods across multiple mRNA vaccine products, including SPIKEVAX™ (mRNA-1273, BLA 125752), mNEXSPIKE™ (mRNA-1283, BLA 125835), MRESVIA™ (mRNA-1345, BLA 125796), and mRNA-1010 (this submission). These methods are validated using representative material and applied to other products with the same manufacturing processes, formulations, and matrices. The sponsor categorized these platform methods under two categories: sequence-agnostic (validated with a single product) and sequence-specific (validated for each product). However, their classification is more nuanced, as detailed in each method's review narrative below.

For this submission, several mRNA-1273 validations and (b) (4) validation were referenced for the mRNA-1010 methods. The products share the same RNA (b) (4), total RNA content, (b) (4) DP target RNA and lipid concentrations.

The platform methods have undergone minor changes since the mRNA-1273 validations, that do not impact the validation status. The methods were confirmed to be applicable to mRNA-1010 through batch analyses and product-specific verification activities.

Prior Submissions Referenced

- 125752/0 – original BLA for SPIKEVAX (mRNA-1273)
- 125752/31 – addition of Moderna (b) (4) site
- 125752/74 – addition of (b) (4) site
- 125752/201 – addition of Moderna (b) (4) site
- (b) (4) – original BLA for (b) (4)
- 125796/0 – original BLA for MRESVIA (mRNA-1345)

Documents Reviewed

1.2 Cover Letters

3.2.S.2 Manufacturer(s)

3.2.S.4 Control of Drug Substance (Analytical Procedures, Validation of Analytical Procedures)

3.2.P.3.1 Manufacturer(s)

3.2.P.5 Control of Drug Product (Analytical Procedures, Validation of Analytical Procedures)

3.2.R Regional Information

Amendments – see Correspondence History below

Correspondence History

Table 2. Information Request submitted by DBSQC and Amendment Correspondence

Correspondence*	Date	Summary of Request or Submission Content
IR #14	March 17, 2026	Requested SOPs for particulate matter and deliverable volume, SOP deficiencies, and validation of (b) (4)
IR #16 (CMC Stats)	March 20, 2026	Question about purity assay (SOP-5401) validation
Amendment 26	March 25, 2026	Response to IR #16
Amendment 27	March 30, 2026	Response to IR #14; SOP-0509, SOP-5183
IR #19 (CMC Stats)	March 26, 2026	Requested validation missing from Amendment 26
Amendment 29	March 31, 2026	Response to IR #19; RPT-78652
IR #42	May 12, 2026	Requested quantitative validation of (b) (4) -specific validation of multiple methods
Amendment 59	May 22, 2026	(b) (4) batch analyses
Amendment 60	May 22, 2026	Response to IR #42
IR #51 (CMC Stats)	June 1, 2026	Requested additional SOP-5401 validation
IR #54	June 3, 2026	Requested product-specific parameter form (FRM-1747) for SOP-2187, SOP-5401 verification of mRNA-1010 DP, demonstration that splitting not an issue in SOP-5401
Amendment 77	June 16, 2026	Response to IR #54; (b) (4)
IR # 64	June 18, 2026	Requesting SST modifications for (b) (4) (SOP-0998)
Amendment 86	June 30, 2026	Response to IR #64
Amendment 87	June 30, 2026	Response to IR #51; RPT-102661
Amendment 88	June 30, 2026	(b) (4) – Module 3
IR #68	July 6, 2026	Requested full reports for validations submitted in Amendment 88
Amendment 90	July 9, 2026	Response to IR #68; RPT-101587, RPT-102424

Review Narrative

1. (b) (4) (Appearance, Deliverable Volume, (b) (4) DP)

Specifications and Methods

There are five (b) (4) methods for (b) (4) DP as shown in the tables below. The SOPs for deliverable volume and (b) (4) were initially omitted from the submission, and they were requested (IR #14) and provided (Amendment 27). The procedures were previously reviewed by (b) (6) and approved within 125752/0. Sufficient details are provided to execute the methods.

Table 3. Matrix of Analytical Tests, Testing Sites, and Associated Materials

Test	Moderna (b) (4)	Moderna (b) (4)	(b) (4)	(b) (4)
Appearance	(b) (4)	DP	DP	--
Deliverable Volume	--	DP	DP	--
(b) (4)				
(b) (4)	--	DP	--	DP
(b) (4)				

Table 4. (b) (4) Method Specifications, General Chapters, and SOPs

Test	Material(s)	Specification	(b) (4) I References	SOP
Appearance	(b) (4) , DP	RNA: Clear, colorless solution, essentially free of visible particulates; (b) (4), DP: White to off-white dispersion. May contain visible, white or translucent product-related particulates	(b) (4)	SOP-0278
Deliverable Volume	DP	(b) (4) 0.38 mL per syringe (each of 5)		SOP-5183
(b) (4)	(b) (4)	(b) (4)		SOP-0279
(b) (4)	DP	(b) (4)		SOP-0509
(b) (4)	(b) (4)	(b) (4)		SOP-0288

Verification

All testing sites have been previously approved for these methods for similar products (STN125752).. Verification of the suitability for testing (b) (4) DP of activities were as follows are summarized in the table below:

Table 5. Summary for Verification reports for (b) (4) Methods

Test (materials tested)	Report	Site	Materials tested to verify method
Appearance (b) (4) DP)	RPT-71378	Moderna (b) (4)	(b) (4), DP
	RPT-17179	Moderna (b) (4)	DP
	QC-MVR-0001	Moderna (b) (4)	DP
	R-2020-VERIF-QC-032	(b) (4)	DP
	RPT-21587	(b) (4)	DP
Deliverable volume (DP)	RPT-17179	Moderna (b) (4)	DP
	REC-2299	(b) (4)	DP

Report	Test	Materials	Sample (Lot)	Design	Criteria	Result
RPT-79262	(b) (4)	(b) (4)	(b) (4)	(b) (4)	(b) (4)	(b) (4)
RPT-79262						
RPT-17179						
RPT-17179						
RPT-17179						
RPT-17179	Dev. Vol.	DP				
RPT-21587	(b) (4)	(b) (4)				
RPT-21587						
RPT-79692						

(b) (4)

In addition, results of MFLUSIVA DP batch analyses performed at (b) (4) all met specifications, demonstrating the suitability of Appearance, Deliverable volume, (b) (4) release testing at this site; similarly results of batch analyses performed at Moderna (b) (4) all met specifications, demonstrating suitability of Appearance, (b) (4) for release of MFLUSIVA RNA, (b) (4). The information provided is sufficient to support suitability of testing performed at Moderna (b) (4), Moderna (b) (4)

(b) (4)

(b) (4)

(b) (4)

[Redacted]

5. Total RNA by (b) (4), DP)

Specifications

The specifications for total RNA are: (b) (4); DP, (b) (4). The (b) (4) specification (b) (4) for other mRNA products.

Method

(b) (4)

[Redacted]

(b) (4)

7. Lipid Identity, Content, and Impurities by (b) (4), DP)

Specifications

The specifications for lipid identity, content, and impurities of (b) (4) DP are:

Table 10. Specifications for Lipid Identity, Content, and Impurities by (b) (4)

Parameter	(b) (4)	DP (b) (4)
Lipid Identity (SM-102, cholesterol, DSPC, PEG2000-DMG)	(b) (4)	(b) (4)
SM-102 Content		
Cholesterol Content		
DSPC Content		
PEG2000-DMG Content		
Individual Impurities		
Total Impurities		

The specifications are the same as those for other mRNA products except for impurities, which were tightened from (b) (4) area for (b) (4) DP, respectively.

Method

(b) (4)

(b) (4)

10. mRNA Purity by (b) (4) (DP)

Specifications

The specifications for mRNA purity (b) (4) of DP are consistent with other mRNA products:

Table 15. Specifications for mRNA Purity by (b) (4) (DP)

Parameter	Specification
mRNA Purity	(b) (4)
(b) (4)	(b) (4)
	(b) (4)

Method

(b) (4)

Platform Method Rationale and Validation

(b) (4)

(b) (4)

11. Identity and (b) (4) by (b) (4) (DP)

Specifications

The specifications for identity and (b) (4) of DP are:

Table 19. Specifications for Identity and (b) (4) by (b) (4) (DP)

Parameter	Specification
Identity	(b) (4)
(b) (4)	(b) (4)

Method

(b) (4)

Platform Method Rationale and Validation

(b) (4)

(b) (4)

(b) (4)

All criteria were met, demonstrating suitability of the DP test performed at (b) (4)

With all acceptance criteria met, the method has been validated for mRNA-1010 DP testing at both sites.