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Our STN: BL 125869/0

**LATE-CYCLE
MEETING MEMORANDUM**

ModernaTX, Inc.
Attention: (b) (6)
325 Binney Street
Cambridge, MA 02142

Dear (b) (6) :

Attached is a copy of the memorandum summarizing your June 5, 2026, Late-Cycle Teleconference with CBER. This memorandum constitutes the official record of the teleconference. If your understanding of the teleconference outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER in writing as soon as possible.

Please include a reference to STN 125869/0 in future submissions related to the subject product.

If you have any questions, please contact (b) (6)

by email.

Sincerely,

(b) (6)

Office of Vaccines Research and Review
Center for Biologics Evaluation and Research

Late-Cycle Meeting Summary

Meeting Date and Time: June 5, 2026, 1:00 PM – 2:00 PM EDT
Application Number: BLA 125869/0
Product Name: Influenza Vaccine, mRNA (MFLUSIVA)
Proposed Indication: For active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B represented in the vaccine in persons 50 years of age and older.
Applicant Name: ModernaTX, Inc.
Meeting Chair: (b) (6)
Meeting Recorders: (b) (6)

FDA ATTENDEES

(b) (6)

David C. Kaslow, M.D.
(b) (6)

(b) (6)

APPLICANT ATTENDEES

(b) (6)

(b) (6)

BACKGROUND

BLA 125869/0 was submitted on December 5, 2025, for Influenza Vaccine, mRNA.

Proposed indication: for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B represented in the vaccine in persons 50 years of age and older.

PDUFA goal date: August 5, 2026

In preparation for this meeting, FDA issued the Late-Cycle Meeting Materials to Moderna on June 3, 2026. Advisory Committee Briefing Materials were issued to Moderna on June 9, 2026.

DISCUSSION

1. Discussion of Substantive Review Issues

Each issue will be introduced by FDA and followed by a discussion.

A. B/Victoria Correlate of Risk (CoR) and Effectiveness

FDA's review of the B/Victoria hemagglutination inhibition (HAI) CoR in Study P304 has not demonstrated a statistically meaningful correlation (hazard ratio (b) (4); 95% CI: (b) (4)). Microneutralization (MN) superiority data alone, without a formal disease-endpoint CoR analysis, are insufficient to infer effectiveness against B/Victoria.

Moderna confirmed they cannot complete the MN CoR analysis prior to the PDUFA action due date and proposed submitting this analysis as a Postmarketing Commitment (PMC) by December 31, 2026. FDA requested confirmation that this will be submitted as a 506B PMC, which Moderna confirmed during the meeting.

Because the MN CoR data will not be available prior to the PDUFA goal date, the residual uncertainty regarding vaccine effectiveness against B/Victoria may be considered during FDA's review of the proposed labeling.

B. Influenza A H1N1 Correlate of Risk Analysis

FDA has reviewed Moderna's May 8, 2026, amendment regarding the CoR analysis for the A/H1N1 strain in support of the accelerated approval licensure pathway. The central issue is a statistically significant interaction between A/H1N1 HAI titer and the vaccine group. This interaction indicates that predicting disease risk from HAI titer alone requires knowing not only the titer value but also which vaccine the subject received, suggesting that the HAI titer-to-risk relationship may not be consistent across vaccine groups.

Given these observed differences, FDA cannot rule out that HAI titer may not function as a reliable, vaccine-agnostic CoR for the A/H1N1 strain. The primary concern is whether this interaction precludes using HAI titer as the immunological surrogate endpoint underpinning Accelerated Approval, since this regulatory pathway depends on the validity and predictive reliability of such a surrogate. Moderna is expected to directly address whether the statistically significant interaction undermines this foundational assumption. An IR was sent to Moderna requesting additional data on June 8th. Moderna submitted their responses under amendment 75, currently under FDA review.

To further evaluate the comparative effectiveness of mRNA-1010 against the active comparator, Fluzone HD, FDA anticipates issuing a formal information request (IR) for additional analyses. This request will seek supplementary evidence to better characterize and support the effectiveness of mRNA-1010 relative to Fluzone HD, particularly as it pertains to adults 65 years of age and older.

A timely and substantive response to this forthcoming IR is critical to FDA's ability to evaluate whether a regulatory action under the Accelerated Approval pathway for MFLUSIVA is appropriate in this age group. Failure to adequately and promptly address this concern could significantly affect the review timeline and pathway eligibility for this indication. Moderna acknowledged and committed to providing timely responses to future information requests regarding this topic.

C. Postmarketing Requirement (PMR) Study Design (P910)

As a condition of BLA 125869/0 approval, Moderna is required to conduct a PMR study, mRNA-1010-P910, titled "A Pragmatic, Randomized Study to Evaluate Relative Vaccine Effectiveness of mRNA-1010 Versus High-Dose Influenza Vaccine in U.S. Adults ≥ 65 Years." The study is designed to assess the relative vaccine effectiveness (rVE) of MFLUSIVA compared with an active high-dose influenza vaccine comparator (Fluzone HD) and is currently under review. A central element of the review has been the proposed noninferiority (NI) margin and the study initiation timeline, both of which were discussed during the Late Cycle Meeting.

Two principal concerns were raised during review discussions:

1. Regarding the NI margin: Moderna's initial protocol synopsis proposed a margin of lower bound (LB) $> -20\%$, which FDA did not find acceptable; FDA's recommended margin is LB $> -10\%$. In the subsequently submitted full study protocol, Moderna proposed LB $> -15\%$, citing operational feasibility. While a margin of -15% may be acceptable, FDA communicated that if the rVE point estimate favors the active comparator and the upper limit of the 2-sided confidence interval (CI) of the rVE (MFLUSIVA/active comparator) is less than 0% , this finding – indicating inferiority of MFLUSIVA relative to the active comparator – will be considered a major review issue, notwithstanding satisfaction of the NI criterion. Moderna acknowledged that a study result with a rVE point estimate that favors the active comparator and an upper limit of the 2-sided CI of the rVE less than 0% will be considered a major review issue by FDA.
2. Regarding study timelines: FDA recommended initiation of the randomized stage (Stage 2) during the 2026–2027 influenza season, whereas Moderna's protocol proposes Stage 2 initiation in September 2027. FDA sought confirmation that Stage 1 will be initiated in August 2026 as proposed and requested that Moderna provide documentation of the executed study agreement with Kaiser Permanente Northern California (KPNC), with a target submission date of June 15, 2026, prior to or concurrent with BLA approval. During the meeting, Moderna indicated that the KPNC agreement had already been approved. FDA additionally noted that further feedback and information requests related to the proposed study design may be communicated in subsequent correspondence.

D. Inadequate Justification for Proposed Minimum Effective Delivered Dose (EDD) per Influenza Strain

During the LCM telecon, several CMC review issues were identified and discussed between FDA and Moderna. These issues focused on the adequacy of the minimum effective delivered dose (EDD) determination for each influenza strain (an EDD that will elicit antibody responses comparable to those observed with the mRNA-1010-P304 clinical trial material lots).

An IR regarding the minimum EDD was issued by FDA on May 29, 2026, and Moderna's response was received on June 4, 2026. During the LCM telecon, FDA indicated that the proposed new minimum EDD per influenza strain is currently under review, and that Moderna must provide a robust, statistically supported data package demonstrating that the newly calculated minimum EDD elicits antibody responses comparable to those observed with the mRNA-1010-P304 clinical trial material (CTM) lots, accompanied by a corresponding shelf-life justification. FDA also identified a discrepancy in Moderna's June 4, 2026 submission under Amendment 70, which referenced a proposed end-of-shelf-life (EoSL) specification of EDD (b) (4). Based on the applicable release specifications for RNA content and (b) (4), and the EoSL specification for RNA Purity, it was noted that the correct proposed EoSL specification should be EDD = (b) (4). Moderna confirmed that the EDD = (b) (4) calculated by the FDA is correct. FDA also inquired whether Moderna's use of a higher EDD value (b) (4) rather than (b) (4) was based on the assumption that the probability of manufacturing a drug product lot at the minimum release specification is negligible, as supported by a Monte Carlo simulation. Moderna confirmed that this was the case.

FDA followed up by asking whether the Monte Carlo simulation provides probabilities of obtaining lots at different release values and indicated that this simulation may need to be reviewed further. FDA also noted that, with the exception of study mRNA-1010-P304, all studies cited in amendment 70 to support the minimum EDD - including CRID-004 – appear to have been conducted in participants 65 years of age or younger, and requested that Moderna confirm this understanding. Moderna committed to provide a response.

Regarding the clinical study supporting the EDD bridging approach, FDA raised questions about Study (b) (4). Specifically, FDA noted that there was (b) (4)

(b) (4)
Moderna indicated that no additional testing was performed and that the approach relies on stability data from their mRNA-1010 program. Additional information requests

may be sent once confirmation regarding lot storage temperature is received from Moderna.

FDA identified an issue with the updated DP specifications submitted on June 2, 2026 in Amendment 65. Moderna indicated “N/A” as the stability acceptance criteria for the EoSL for the (b) (4) test method. However, Moderna had previously committed to generating both (b) (4) results and quantitative (b) (4) data to assess maintenance of functional performance over the proposed refrigerated shelf life and to support comparability across lots and strains. FDA requested that Moderna revise the stability specification for (b) (4) to read “Report results only” and submit an updated post-approval stability protocol in Section 3.2.P.8.2 that include the (b) (4) test. This action item is required to ensure consistency between Moderna’s prior commitments and the submitted stability program.

2. Discussion of Minor Review Issues

A. Data Integrity Issues

A communication was sent to Moderna on May 22, 2026, (IR #47) to address a series of outstanding dataset deficiencies spanning several clinical data domains. This communication raised concerns about missing, inconsistent, or improperly reported data across multiple CDISC-standard domains (e.g., MB, SV, CE, FACE, VS, CM, PR, and SUPPDM), as well as inadequate documentation and validation of electronic diary (eDHT) devices used for remote data collection. Moderna was requested to provide corrections, resubmissions, and forward-looking commitments to improve data quality and standardization in future BLA/sBLA submissions, with a response received June 2, 2026. These responses were under review at the time of the Late Cycle Meeting.

B. Method Validation for SOP-5401 (RPT-78652)

The submitted validation data for the quantitative purity assay (SOP-5401) are insufficient in three key areas: the claimed validated range is not supported by available linearity data, intermediate precision has not been demonstrated across the intended range at multiple purity levels, and inter-laboratory comparability between the (b) (4) sites has not been adequately established. Comprehensive additional testing — including range-appropriate linearity, multi-level intermediate precision, and either full validation or a robust transfer study at the (b) (4) site — is required before the assay can be considered adequately validated. An information request was issued on June 1, 2026, with a response expected by June 30, 2026. Moderna confirmed that the requested method Validation for SOP-5401 was completed and would be submitted to the BLA by close of business on June 5, 2026.

3. Additional Applicant Data

Moderna had no additional data to share.

4. Pending Information Requests

The following Information requests had pending responses as of June 5, 2026:

- IR #51 – Method Validation for SOP-5401 (RPT-78652) (referencing Amendment #51), Sent June 1, 2026, Due June 30, 2026
- IR #52 – In Process Support Testing, Sent June 2, 2026, Due June 11, 2026
- IR #53 – PPQ and Media Fill Summary Reports, Shipping and (b) (4) Validation, and Container Closure, Sent June 2, 2026, Due June 10, 2026
- IR #54 - Analytical Chemistry Procedures and Validation Follow-up, Sent June 3, 2026, Due June 16, 2026

5. Discussion of Upcoming Advisory Committee Meeting

A Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting is scheduled for June 18, 2026, to discuss BLA 125869/0. FDA stated that the FDA VRBPAC Briefing Document is expected to be shared with Moderna by June 5, 2026, for review, and acknowledged Moderna's plan to submit comments by start of business on June 9, 2026. FDA noted that final questions for the Advisory Committee were expected to be posted two days prior to the meeting and would be made available at <http://www.fda.gov/AdvisoryCommittees/Calendar/default.html>. Moderna was reminded that the VRBPAC meeting is a public meeting, and that all materials submitted to FDA for the briefing package would be made publicly available in accordance with FDA's standard procedures.

6. Postmarketing Requirements/Postmarketing Commitments

Regarding PMRs and PMCs, the following were discussed:

For Study mRNA-1010-P910, *"A Pragmatic, Randomized Study to Evaluate Relative Vaccine Effectiveness of mRNA-1010 Versus High-Dose Influenza Vaccine in U.S. Adults ≥65 Years,"* the full protocol was submitted to IND 27460 on May 22, 2026. Outstanding issues regarding the noninferiority (NI) margin and study initiation timeline were discussed under Agenda Item 2. PMR study target details will be communicated to Moderna no later than June 24, 2026. Moderna proposed submitting the B/Victoria MN CoR Analysis as a PMC by December 31, 2026. FDA acknowledged this proposal during the Late Cycle Meeting and noted that PMC study target details will be communicated to Moderna by July 6, 2026. No additional PMRs or any safety-related PMCs had been identified at the time of the Late Cycle Meeting.

7. Review Plans

- VRBPAC Meeting: June 18, 2026
- PMR study target details to Moderna: June 24, 2026
- Final "wave 3" CMC Amendment expected from Moderna: June 30, 2026
- PMC study target details to Moderna: July 6, 2026

- PDUFA Action Due Date: August 5, 2026

8. Applicant Questions

There were no additional applicant questions raised during the meeting.

9. Wrap-up and Action Items

FDA thanked Moderna representatives for their participation in the Late Cycle Meeting discussion and asked Moderna to send the list of participants by email. FDA noted that the official summary of the meeting will be sent to Moderna on or before July 3, 2026.

This application has not yet been fully reviewed by the signatory authorities, Division Directors and Review Committee Chair and therefore, this meeting did not address the final regulatory decision for the application.