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Our STN: BL 125869/0

**MID-CYCLE COMMUNICATION
SUMMARY**
May 6, 2026

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

Dear (b) (6) :

Attached is a copy of the summary of your April 6, 2026, Mid-Cycle Communication 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 as soon as possible.

Please include a reference to STN 125869/0 in your 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

Mid-Cycle Communication Teleconference Summary

Application Type and Number:

BLA 125869/0

Product Name:

Influenza Vaccine, mRNA (MFLUSIVA)

Proposed Indication for Use:

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:

ModernaTX, Inc.

Meeting Date & Time:

April 6, 2026; 1:00 – 2:00 PM EST

(b) (6) :
(b) (6)

(b) (6)
(b) (6)

Attendees:

Moderna

(b) (6)

FDA

(b) (6)

David C. Kaslow, MD

(b) (6)

Background/Regulatory History:

FDA began the meeting by summarizing the following key regulatory milestones and background info:

- Moderna submitted STN 125869 on December 5, 2025.
- CBER issued a Refusal to File letter on February 3, 2026. Moderna responded with a proposed two-track approval strategy seeking traditional approval for adults 50 through 64 years of age based on existing efficacy and safety data, and accelerated approval for adults 65 years of age and older based on immunogenicity data with a postmarketing comparative efficacy study as a condition.
- On February 17, 2026, CBER issued a [Filing Notification Letter with Deficiencies Identified](#), detailing CBER's concerns that Study P304 used Fluarix as the comparator rather than an ACIP-preferred vaccine for older adults, and that no FDA-validated immunological surrogate exists to support traditional approval for that age group.

Discussion Summary:

- 1. Any significant issues/major deficiencies, categorized by discipline, identified by the Review Committee to date.**

Regulatory/Clinical/Stats Issues

Accelerated Approval Criteria Assessment (65 years of age and older)

FDA communicated to Moderna that the assessment of whether MFLUSIVA meets the criteria for accelerated approval for use in individuals ≥ 65 years of age includes ongoing evaluation of the following:

- **Criterion #2 (Meaningful Advantage over Existing Therapy):** Evaluation of whether the mRNA-manufacturing technology and strain matching capabilities provide a meaningful advantage over existing therapies.
- **Criterion #3 (Reasonably Likely Surrogate Endpoint):** Assessment of whether HAI titers are surrogate endpoints reasonably likely to predict clinical benefit, especially regarding the B/Victoria strain. Alternative endpoints or additional data that support this criterion may be requested.
- **Criterion #4 (Postmarketing Requirement Study; PMR):** Assessment of the acceptability and feasibility of the proposed timeline for submitting the PMR study synopsis with associated milestone dates by May 8, 2026, and the full protocol to enable substantive review and agreement prior to the anticipated Accelerated Approval Regulatory Action Due Date (ADD), i.e., PDUFA goal date, of August 5, 2026.

Additional discussion of Criterion #3 (surrogate endpoint reasonably likely to predict clinical benefit):

FDA indicated that review of the Correlate of Risk (CoR)/Correlate of Protection (CoP) analysis is ongoing and discussed concerns regarding use of HAI titers as a surrogate endpoint reasonably likely to predict clinical benefit for the B/Victoria strain, including issues with statistical methodology and sensitivity analyses.

- FDA noted that in the P304 study, while HAI titers appear to correlate with disease risk for the A/H1N1 and A/H3N2 strains, there was no meaningful correlation with disease risk for the B/Victoria strain. This lack of correlation cannot be explained solely by insufficient statistical power. In contrast, the P301 study demonstrated correlation between HAI titers and disease risk for all three strains (A/H1N1, A/H3N2, and B/Victoria). Notably, the number of cases observed for the B/Victoria strain was similar in both the P301 and P304 studies.
- In Study P304, the relationship between HAI titers and protection differed significantly by vaccine group for the A/H1N1 strain but not for the A/H3N2 or B/Victoria strains; this strain-specific finding suggests that the titer-to-protection relationship may not be similar between the two vaccines for the A/H1N1 strain, undermining a key assumption of the immunogenicity bridging approach for this strain and raising questions about whether a noninferior HAI titer response can be equated with noninferior clinical protection.
- Moderna was advised that an information request regarding these issues is forthcoming.

Moderna confirmed the low incidence of influenza B cases across its studies but noted that efficacy results from Study P304 were consistent with those for influenza A. Moderna committed to providing a detailed point-by-point assessment after receiving the information request.

Additional discussion of Criterion #4 (regarding the proposed Postmarketing Requirement (PMR) Study)

FDA communicated that the review team is currently assessing the acceptability and feasibility of the proposed submission timeline for the PMR study synopsis (proposed submission by May 8, 2026) and full protocol to allow for substantive review and agreement prior to the anticipated Accelerated Approval ADD of August 5, 2025.

- FDA requested that Moderna confirm the anticipated submission date for their postmarketing requirement (PMR) study synopsis and emphasized that the synopsis must contain sufficient detail to

facilitate a substantive review. FDA also requested that Moderna incorporate study milestones and corresponding milestone dates into the synopsis submission.

- Moderna noted that a partner has been identified to conduct the AA PMR study. Moderna also noted that a detailed PMR protocol with associated milestones will be submitted within the following week, with plans to collaborate with their partner to finalize and submit the protocol in May 2026.

Discussion of Quadrivalent to Trivalent Data Bridging (65 years of age and older)

FDA informed Moderna that the review team continues to assess the appropriateness of using immunogenicity data from the quadrivalent mRNA-1010 formulation (50 µg) evaluated in Study P303 Part C to support approval of the trivalent formulation, including potential comparability concerns such as enhancement or interference effects from the additional B strain.

- FDA indicated that an information request would be forthcoming to request justification and evidence supporting this approach.

Moderna noted that study P304 demonstrated relative vaccine efficacy versus the comparator vaccine and noted that HAI geometric mean titers (GMTs) for the B/Victoria strain are comparable to those observed for quadrivalent (QIV) and trivalent (TIV) influenza vaccines.

Traditional Approval Assessment (50 through 64 years of age)

FDA expressed concern regarding the uncertainty in the estimated relative vaccine efficacy (rVE) of mRNA-1010 compared with the active comparator for the B/Victoria strain in the 50- through 64-year age group due to the low number of influenza B cases accrued. Additionally, FDA discussed that Moderna had not yet been able to demonstrate HAI as a correlate of risk (CoR) for the B/Victoria strain in this age group. Consequently, FDA lacks confidence in the data submitted to demonstrate the efficacy of MFLUSIVA against the B/Victoria strain in the target population.

Moderna's Totality of Data Approach

Moderna acknowledged that individual studies lack sufficient statistical power to evaluate each strain individually. Moderna proposed presenting the totality of data from Studies P301, P302, and P304, citing geographic and season-to-season variability in influenza patterns. Moderna indicated their intention is to integrate all available data to build a more comprehensive narrative. Moderna's proposed totality of data includes

cellular and humoral immunogenicity data from Studies P301 and P302, and microneutralization data. Moderna noted that Study P304 was not conducted during a season where there was substantial B/Victoria circulation and suggested this timing may have impacted their results.

Microneutralization Data Discussion

To address the uncertainty in the estimated rVE of mRNA-1010 against the B/Victoria strain in the 50 through 64 year age group, and the absence of HAI as an established correlate of risk for the B/Victoria strain, FDA and Moderna discussed whether microneutralization data could serve as an additional immunogenicity endpoint to provide the strain-specific supportive evidence needed to substantiate the vaccine's efficacy against influenza B. FDA clarified that microneutralization data in isolation, without demonstrated correlation to clinical disease outcomes is inadequate. FDA requested that Moderna provide a specific proposal for how they intend to use microneutralization data to support their application. FDA noted that the HAI and microneutralization comparison was conducted in a limited subset of 500 participants and demonstrates only the relationship between the two assays, rather than a correlation with the disease endpoint. FDA indicated that if Moderna can demonstrate that microneutralization correlates with the disease endpoint (comparing mRNA-1010 with the active comparator), this may provide a path forward to address the concerns regarding the B/Victoria strain.

Moderna noted that they were able to demonstrate positive efficacy for B/Victoria in Study P304. Moderna reported that microneutralization studies were conducted across Studies P303 Parts A, B, and C, and P304, with results demonstrating high correlation, although they acknowledged that microneutralization is a more variable assay compared with HAI. Moderna proposed to pool all microneutralization data across studies, noting that there was strong overall correlation across their data. However, Moderna expressed uncertainty about whether an analysis correlating microneutralization with rVE in Study P304 would produce results meaningfully different from those obtained using HAI, given the close correlation between the two assays and the geographic variability in Study P304. In response to FDA's request, Moderna indicated they would discuss further with their team, but noted such an analysis would be challenging.

CMC Issues

FDA informed Moderna that an information request would be forthcoming in follow-up to the technical working group meeting (held on April 1, 2026) regarding the approach to evaluating potency of mRNA-1010 Drug Product. Topics addressed in the TWG meeting included:

- Effective delivered dose (EDD)

- Moderna acknowledged that Effective delivered dose (EDD) by itself is not sufficient to serve as a potency assessment that ensures the vaccine will elicit comparable immune responses to the CTM lots used to demonstrate clinical efficacy.
- Generation of *in vivo* immunogenicity data for the new strains.
- Use of (b) (4) to ensure (b) (4) comparability of new strains to previous strains:
 - Qualification of the reference materials used in (b) (4) .
 - Characterization of the strain-specific (b) (4) used in (b) (4) .

FDA noted that only 2 of the 3 influenza strains for the 2026-2027 season were assessed in the immunogenicity study submitted on March 20, 2026, in amendment 18. Moderna acknowledged this and indicated that these were preliminary studies. Moderna stated that immunogenicity studies representing all 3 strains for the 2026-2027 season will be submitted in a later submission.

2. Information regarding major safety concerns.

FDA indicated that no major safety concerns have been identified to date; however, the safety data submitted are still being independently verified. At the time of this meeting, FDA was unable to comment on any impact the higher frequency of the solicited adverse reactions and increased reactogenicity observed in the mRNA-1010 group may have on the overall benefit-risk assessment of mRNA-1010.

3. Preliminary Review Committee thinking regarding:

a. Risk management

FDA indicated that review of the Risk Management Plan is ongoing.

b. The potential need for any postmarketing requirement(s) (PMRs), and/or safety-related PMCs

Moderna was informed that the review team is currently evaluating the acceptability and feasibility of the proposed submission timeline for the Accelerated Approval PMR study synopsis (proposed submission by May 8, 2026) and final protocol. This assessment will determine whether the timeline allows sufficient time for substantive review and agreement before the anticipated Accelerated Approval ADD of August 5, 2026. The need for any additional PMRs or safety-related PMCs was still being evaluated by FDA at the time of this meeting.

c. The ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk.

FDA indicated that the review team has not yet determined whether CBER's Sentinel Program and adverse event reporting will provide sufficient information regarding product risk.

4. Any information requests sent, and responses not received.

FDA confirmed that Moderna had responded to all information requests issued as of the time of the Midcycle communication. Moderna expressed their willingness to continue engaging through information requests and emphasized their commitment to work collaboratively with FDA to move the application forward in its review process.

5. Any new information requests (IRs) to be communicated.

FDA summarized the following general topics for potential IRs to be issued following the Midcycle communication:

- Comparability of immunogenicity data from trivalent and quadrivalent formulations of mRNA-1010.
- Assessment of HAI titers as reasonably likely surrogate endpoints for the influenza B/Victoria strain.
- STDM Clinical Dataset questions.
- CMC questions in follow-up to the TWG meeting held on April 1, 2026.

6. Proposed date(s) for the Late-Cycle meeting (LCM).

FDA indicated that details regarding the late cycle meeting will be communicated once a decision has been reached regarding whether STN 125869/0 will be discussed at an Advisory Committee (AC) meeting. FDA expressed their intent to send the LCM materials to Moderna approximately 10 calendar days in advance of the LCM.

- Moderna was assured that if these timelines change, updates will be communicated as soon as possible.

7. Updates regarding plans for the AC meeting.

Moderna was informed that the decision whether to discuss STN 125869/0 at an AC meeting is under internal discussion, and that consideration is anticipated to continue into May 2026. Per PDUFA VII Performance Goals, if the application will be discussed at an AC FDA intends to convene that AC no later than 6 weeks prior to the PDUFA goal date and will notify Moderna once a decision is made.

8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates.

FDA indicated that initial labeling comments will be communicated no later than July 6, 2026, and that any postmarketing requirement and postmarketing commitment requests will be communicated no later than June 24, 2026, and July 6, 2026, respectively.

9. Discuss status of inspections (GMP, (b) (6), GLP) including issues identified that could prevent approval.

FDA informed Moderna that there are no inspections of manufacturing facilities planned at this time, and that clinical site selection for FDA's (b) (6) program will be communicated shortly.