U.S. FOOD & DRUG ADMINISTRATION

Our STN: BL 125835/0

BLA APPROVAL
May 30, 2025

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

Dear (b) (6):

Please refer to your Biologics License Application (BLA) received September 30, 2024, submitted under section 351(a) of the Public Health Service Act (PHS Act) for COVID-19 Vaccine, mRNA (MNEXSPIKE).

LICENSING

We have approved your BLA for COVID-19 Vaccine, mRNA (MNEXSPIKE) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, COVID-19 Vaccine, mRNA (MNEXSPIKE) under your existing Department of Health and Human Services U.S. License No. 2256. COVID-19 Vaccine, mRNA (MNEXSPIKE) is indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). MNEXSPIKE is approved for use in individuals who have been previously vaccinated with any COVID-19 vaccine and are 65 years of age and older, or 12 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT04813796, NCT05137236, NCT05815498, NCT04927065, and NCT04649151.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture COVID-19 Vaccine, mRNA at your facility located at (b) (4). The final product will be manufactured, filled, labeled, and packaged at the following facility locations:

- (b) (4)
- (b) (4)

You may label your product with the proprietary name MNEXSPIKE and market it in cartons containing 1, 2 or 10 single-dose (0.2 mL) prefilled syringe(s).

ADVISORY COMMITTEE

We did not refer your application to the Vaccines and Related Biological Product Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for COVID-19 Vaccine, mRNA shall be 12 months from the date of manufacture when stored in the commercial container-closure system at the recommended long-term storage condition of -40ºC to -15ºC that may include up to 90 days of storage at 2°C to 8°C and up to 24 hours at room temperature (15°C to 25ºC). The date of manufacture shall be defined as the start date of labeling and packaging operations. Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency. The dating period for your drug substance shall be (b) (4) months when stored in the approved container-closure system at (b) (4)

COMPARABILITY PROTOCOL

Under 21 CFR 601.12(e), approval of a comparability protocol may justify a reduced reporting category for a particular change. In your annual report (21 CFR 601.12(d)), you should report information confirming that the change(s) meet(s) the requirements specified in your approved comparability protocol. Include the information described in 21 CFR 601.12(d)(3).

FDA LOT RELEASE

Please submit final container samples of the product in final containers together with protocols showing results of all applicable tests. You may not distribute any lots of your product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to (b) (6) , electronically through the eBPDR web application or at the address below.

Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations :

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of COVID-19 Vaccine, mRNA, or in the manufacturing facilities.

LABELING

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.
We hereby approve the draft content of labeling including Package Insert and Patient Package Insert, submitted under amendment 64, dated May 30, 2025, and the draft package and container labels submitted under amendment 64, dated May 30, 2025.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert and Patient Package Insert submitted on May 30, 2025. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

PACKAGE AND CONTAINER LABELS

Please electronically submit final printed package and container labels identical to the package and container labels submitted on May 30, 2025, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/downloads/drugs/guidancecompliance regulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125835 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to (b) (6) at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). In addition to the reporting requirements in 21 CFR 600.80, you must submit adverse experience reports for myocarditis and pericarditis as 15-day expedited reports to the Vaccine Adverse Event Reporting System (VAERS) at https://vaers.hhs.gov/. Myocarditis and pericarditis reports must be submitted as 15-day expedited reports for three years following the date of product licensure. You must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting,

please refer to the guidance for industry *Providing Submissions in Electronic Format — Postmarketing Safety Reports for Vaccines* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports-vaccines. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.
For information on the postmarketing safety reporting requirements for combination products as described in 21 CFR 4, Subpart B, and the dates by which combination product applicants must comply with these requirements, please refer to the Postmarketing Safety Reporting for Combination Products webpage available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies for ages <12 years for this application because this product is ready for approval for use in adults and children over 12 years of age and the pediatric studies in <12 years of age have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) are required postmarketing studies. The status of these postmarketing studies must be reported according to 21 CFR 601.28 and section 505B(a)(4)(C) of the FDCA. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

Label your annual report as an "**Annual Status Report of Postmarketing Study Requirement/Commitments**" and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. These required studies are listed below:

1. Deferred pediatric study under PREA (mRNA-1283-P302) to evaluate the safety and effectiveness of MNEXSPIKE in infants and children 6 months to <12 years of age for the prevention of COVID-19.

Final Protocol Submission: January 31, 2026

Study Completion Date: December 31, 2029

Final Report Submission: June 30, 2030

2. Deferred pediatric study under PREA (mRNA-1283-PXXX) to evaluate the safety and effectiveness of MNEXSPIKE in neonates and infants < 6 months of age for the prevention of COVID-19.

Final Protocol Submission: March 31, 2030

Study Completion Date: December 31, 2034

Final Report Submission: June 30, 2035

Submit the protocols to your IND 27196, with cross-reference letters to this BLA, STN BL 125835 explaining that these protocols were submitted to the IND.

Submit final study reports to this BLA STN BL 125835. In order for your PREA PMRs to be considered fulfilled, you must submit and receive approval of either an efficacy or a labeling supplement. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated as:

- **Required Pediatric Assessments**

We note that you have fulfilled the pediatric study requirement 12 through 16 years of age for this application.

POSTMARKETING REQUIREMENTS UNDER SECTION 505(o)

Section 505(o) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

We have determined that an analysis of spontaneous postmarketing adverse events reported under section 505(k)(1) of the FDCA will not be sufficient to assess the known serious risks of myocarditis and pericarditis.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, we have determined that you are required to conduct the following studies:

3. A postmarketing retrospective cohort study utilizing commercial and Medicare claims databases to evaluate the occurrence of myocarditis and pericarditis following administration of MNEXSPIKE in the United States (Study mRNA-1283-P901).

   We acknowledge the timetable you submitted on May 28, 2025, which states that you will conduct this study according to the following schedule:

   Final Protocol Submission: June 30, 2025

   Study Completion Date: March 30, 2029

   Final Report Submission: September 30, 2029

4. A postmarketing retrospective cohort study using administrative claims and health system medical records to evaluate long-term sequelae of myocarditis following administration of MNEXSPIKE compared to myocarditis in patients who have not received a COVID-19 vaccine (Study mRNA-1283-P904). Participants will have at least five years of follow-up for long-term outcomes of myocarditis.

   We acknowledge the timetable you submitted on April 4, 2025, which states that you will conduct this study according to the following schedule:

   Final Protocol Submission: November 30, 2025

   Study Completion Date: March 31, 2033

   Final Report Submission: March 31, 2034

Please submit the protocols to your IND 27196, with cross-reference letters to this BLA, STN BL 125835 explaining that these protocols were submitted to the IND. Please refer to the sequential number for each study/clinical trial and the submission number as shown in this letter.

Please submit final study reports to the BLA. If the information in the final study report supports a change in the label, the final study report must be submitted as a supplement to this BLA, STN BL 125835. For administrative purposes, all submissions related to these postmarketing studies required under section 505(o) must be submitted to this BLA and be clearly designated as:

- **Required Postmarketing Correspondence under Section 505(o)**
- **Required Postmarketing Final Report under Section 505(o)**
- **Supplement contains Required Postmarketing Final Report under Section 505(o)**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

You must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing requirement;
- the original milestone schedule for the requirement;
- the revised milestone schedule for the requirement, if appropriate;
- the current status of the requirement (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status for the study or clinical trial. The explanation should include how the study is progressing in reference to the original projected schedule, including, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

We will consider the submission of your annual report under section 506B of the FDCA and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in section 505(o) and 21 CFR 601.70. We remind you that to comply with section 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to periodically report on the status of studies or clinical trials required under section 505(o) may be a violation of FDCA section 505(o)(3)(E)(ii) and could result in regulatory action.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

5. An observational cohort study using administrative claims data to assess maternal and infant outcomes following exposure to MNEXSPIKE during pregnancy (Study mRNA-1283-P902).

   We acknowledge your written commitment as described in your letter of May 28, 2025, as outlined below:

   Final Protocol Submission: August 31, 2025

   Study Completion Date: December 15, 2031

   Final Report Submission: December 15, 2032

6. A Phase 4, Randomized, Observer Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of mRNA-1283 Variant-containing Formulation in Adults 50 to 64 Years of Age Without High-Risk Conditions for Severe COVID-19. (Study mRNA-1283-XXXX).

   We acknowledge the timetable you submitted on May 30, 2025, which states that you will conduct this study according to the following schedule:

   Study Initiation: November 30, 2025

   Interim Results: May 31, 2026

   Study Completion: July 31, 2026

   Final Report Submission: January 31, 2027

   Benefit-Risk Assessment Submission: May 31, 2027

Please submit the clinical protocol to your IND 27196, and a cross-reference letter to this BLA, STN BL 125835 explaining that this protocol was submitted to the IND.

If the information in the final study report supports a change in the label, the final study report must be submitted as a supplement. Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Correspondence**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

Sincerely,

David C. Kaslow, M.D.
Director
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research