



Our STN: BL 125752/0

**BLA APPROVAL**

ModernaTX, Inc.  
Attention: Michelle Olsen  
200 Technology Square  
Cambridge, MA 02139

January 31, 2022

Dear Dr. Olsen:

Please refer to your Biologics License Application (BLA) submitted and received August 24, 2021, under section 351(a) of the Public Health Service Act (PHS Act) for COVID-19 Vaccine, mRNA.

## LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2256 to ModernaTX, Inc., Cambridge, Massachusetts, under the provisions of section 351(a) of the PHS Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product COVID-19 Vaccine, mRNA, which is indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: 04283461; 04405076; 04470427; 04649151; 04796896; 04860297; 04927065

## MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture COVID-19 Vaccine, mRNA, drug substance at ModernaTX, Inc., 1 Moderna Way, Norwood, MA, and Lonza Biologics, Inc., 101 International Drive, Portsmouth, NH. The final formulated product will be manufactured, filled, labeled and packaged at Catalent Indiana, LLC (a subsidiary of Catalent Pharma Solutions, LLC), 1300 S. Patterson Drive, Bloomington, IN, and Baxter BioPharma Solutions, 927 S. Curry Pike, Bloomington, IN.

You may label your product with the proprietary name SPIKEVAX and market it in 10 mL vials containing a maximum of 11 or 15 doses per vial (0.5 mL/dose), in packages of 10 multiple-dose vials.

## **ADVISORY COMMITTEE**

We did not refer your application to the Vaccines and Related Biological Products 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 9 months from the date of manufacture when stored at -25°C to -15°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. 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 at (b) (4) . We have approved the stability protocol in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

## **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 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 the Director, Office of Compliance and Biologics Quality, 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 submitted under amendment 52, dated January 28, 2022, Patient Package Insert submitted under amendment 37, dated December 16, 2021 and the draft carton and container labels submitted under amendment 35, dated December 15, 2021.

## **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 January 28, 2022 and December 16, 2021, respectively. 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.

## **CARTON AND CONTAINER LABELS**

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on December 15, 2021, 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 125752, 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 the Advertising and Promotional Labeling Branch 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), and 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 <http://www.fda.gov/forindustry/electronic submissions gateway/ucm387293.htm>. 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>.

## **MATERIAL THREAT MEDICAL COUNTERMEASURE PRIORITY REVIEW VOUCHER**

We also inform you that you have been granted a material threat medical countermeasure priority review voucher (PRV), as provided under section 565A of the FDCA. This PRV has been assigned a tracking number, PRV BLA 125752. All correspondences related to this voucher should refer to this tracking number.

This voucher entitles you to designate a single human drug application submitted under section 505(b)(1) of the FDCA or a single biologic application submitted under section 351(a) of the Public Health Service Act as qualifying for a priority review. Such an application would not have to meet any other requirements for a priority review. The list

below describes the sponsor responsibilities and the parameters for using and transferring a material threat medical countermeasure PRV.

- The sponsor who redeems the PRV must notify FDA of its intent to submit an application with a PRV at least 90 days before submission of the application and must include the date the sponsor intends to submit the application. This notification should be prominently marked, **“Notification of Intent to Submit an Application with a Material Threat Medical Countermeasure Priority Review Voucher.”**
- This PRV may be transferred, including by sale, by you to another sponsor of a human drug or biologic application. If the PRV is transferred, the sponsor to whom the PRV has been transferred should include a copy of this letter (which will be posted on our website as are all approval letters) and proof that the PRV was transferred. When redeeming this PRV, you should refer to this letter as an official record of the voucher.

For additional information regarding the PRV, see FDA's draft guidance, *Material Threat Medical Countermeasure Priority Review Voucher Program* at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/material-threat-medical-countermeasure-priority-review-vouchers-draft-guidance-industry>. This guidance when finalized, will represent the current thinking of FDA on this topic.

## **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 because the product is ready for approval for use in adults and the pediatric studies 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 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 under section 506B of the FDCA are released or fulfilled. These required studies are listed below:

1. Deferred pediatric study under PREA (Study mRNA-1273-P203) to evaluate the safety and effectiveness of SPIKEVAX in children 12 years through 17 years of age.

Final Protocol Submission: January 31, 2022

Study Completion Date: April 30, 2024

Final Report Submission: July 31, 2024

2. Deferred pediatric study under PREA (Study mRNA-1273-P204) to evaluate the safety and effectiveness of SPIKEVAX in children 6 months through <12 years of age.

Final Protocol Submission: February 28, 2022

Study Completion Date: December 31, 2023

Final Report Submission: March 31, 2024

3. Deferred pediatric study under PREA (Study mRNA-1273-P206) to evaluate the safety and effectiveness of SPIKEVAX in infants < 6 months of age.

Final Protocol Submission: June 30, 2022

Study Completion Date: June 30, 2024

Final Report Submission: December 31, 2024

Please submit the protocols to your IND 19745 with a cross-reference letter to this BLA, STN BL 125752, 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.

Submit final study reports to this BLA, STN BL 125752. 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 Assessment(s)**

#### **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 known serious risks of myocarditis and pericarditis and identify an unexpected serious risk of subclinical myocarditis.

Furthermore, the pharmacovigilance system that FDA is required to maintain under section 505(k)(3) of the FDCA is not sufficient to assess this serious risk.

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

4. Required safety study under Section 505(o) (Study mRNA-1273-P903), entitled “Post-marketing safety of SARS-CoV-2 mRNA-1273 vaccine in the US: Active surveillance, signal refinement and self-controlled risk interval (SCRI) signal evaluation in HealthVerity”, to evaluate the occurrence of myocarditis and pericarditis following administration of SPIKEVAX.

We acknowledge the timetable you submitted on December 14, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: January 31, 2022

Study Completion Date: December 31, 2022

Final Report Submission: June 30, 2023

5. Required safety study under Section 505(o) (Study mRNA-1273-P904), entitled “Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of Spikevax in Europe,” to evaluate the occurrence of myocarditis and pericarditis following administration of SPIKEVAX.

We acknowledge the timetable you submitted on December 14, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: November 4, 2021 (completed)

Study Completion Date: March 31, 2023

Final Report Submission: December 31, 2023

6. Required safety study under Section 505(o) (Study mRNA-1273-P911), entitled “Long-term outcomes of myocarditis following administration of SPIKEVAX (Moderna COVID-19, mRNA-1273),” to evaluate long-term sequelae of myocarditis after vaccination with at least 5 years of follow-up.

We acknowledge the timetable you submitted on December 14, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: April 30, 2022

Study Completion Date: October 31, 2027

Final Report Submission: October 31, 2028

7. Required safety study under Section 505(o) (Study mRNA-1273-P301) substudy to prospectively assess the incidence of subclinical myocarditis following administration of a booster dose of SPIKEVAX in participants 18 years of age and older.

We acknowledge the timetable you submitted on December 14, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: September 14, 2021 (completed)

Study Completion Date: December 31, 2022

Final Report Submission: June 30, 2023

8. Required safety study under Section 505(o) (Study mRNA-1273-P203) substudy to prospectively assess the incidence of subclinical myocarditis following administration of a booster dose of SPIKEVAX in participants 12 years through <18 years of age.

We acknowledge the timetable you submitted on December 14, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: November 12, 2021 (completed)

Study Completion Date: April 30, 2024

Final Report Submission: July 31, 2024

9. Required safety study under Section 505(o) (Study mRNA-1273-P204) substudy to prospectively assess the incidence of subclinical myocarditis following administration of SPIKEVAX in a subset of participants 6 months through <12 years of age.

We acknowledge the timetable you submitted on December 14, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: October 6, 2021 (completed)

Study Completion Date: December 31, 2023

Final Report Submission: March 31, 2024



Please submit the protocols to your IND 19745, with a cross-reference letter to this BLA, STN BL 125752, 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 125752. 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/Guidance/ComplianceRegulatoryInformation/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**

We acknowledge your written commitments as described in your letter of December 14, 2021, as outlined below:

10. Study mRNA-1273-P901, entitled “Real-World Study of the Effectiveness of Moderna COVID-19 Vaccine.”

Final Protocol Submission: December 20, 2021 (completed)

Study Completion Date: January 31, 2024

Final Report Submission: April 14, 2025

11. Study mRNA-1273-P902, entitled “Moderna mRNA-1273 Observational Pregnancy Outcome Study.”

Final Protocol Submission: July 31, 2022

Study Completion Date: September 30, 2023

Final Report Submission: June 30, 2024

12. Study mRNA-1273-P905, entitled “Monitoring safety of Spikevax in pregnancy: an observational study using routinely collected health data in five European countries.”

Final Protocol Submission: November 4, 2021 (completed)

Study Completion Date: March 31, 2023

Final Report Submission: December 31, 2023

Please submit the protocols to your IND 19745 and a cross-reference letter to this BLA, STN BL 125752, 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

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/Guidance/ComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm>.

## **POST APPROVAL FEEDBACK MEETING**

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

Mary A. Malarkey  
Director  
Office of Compliance and Biologics Quality  
Center for Biologics  
Evaluation and Research

Peter W. Marks, M.D., Ph.D.  
Acting Director  
Office of Vaccines Research and  
Review  
Center for Biologics  
Evaluation and Research