Our STN: BL 125796/0

BLA APPROVAL
May 31, 2024

ModernaTX, Inc.
Attention: Laila El Asmar, Ph.D.
325 Binney Street
Cambridge, MA 02142

Dear Dr. El Asmar:

Please refer to your Biologics License Application (BLA) received September 12, 2023, submitted under section 351(a) of the Public Health Service Act (PHS Act) for Respiratory Syncytial Virus Vaccine.

LICENSING

We have approved your BLA for Respiratory Syncytial Virus Vaccine effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce Respiratory Syncytial Virus Vaccine under your existing Department of Health and Human Services U.S. License No. 2256. Respiratory Syncytial Virus Vaccine is indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in individuals 60 years of age and older.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT05127434 and NCT04528719.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Respiratory Syncytial Virus Vaccine drug substance at ModernaTX, Inc., (b) (4) . The final formulated product will be manufactured and filled at (b) (4) ; and be labeled and packaged at the (b) (4)

You may label your product with the proprietary name MRESVIA and market it in single dose (0.5 mL) pre-filled syringes, in cartons of 1 and 10 pre-filled syringes.

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 Respiratory Syncytial Virus Vaccine shall be 18 months from the date of manufacture when stored at -40°C to -15°C, inclusive of up to 1 month storage at 2°C to 8°C. The date of manufacture shall be defined as the date of labeling and packaging of the pre-filled syringes. 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 product under 21 CFR 601.12.

FDA LOT RELEASE

Please submit final container samples of the product 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 Respiratory Syncytial Virus Vaccine, or in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including Package Insert, submitted under amendment 71, dated May 29, 2024 and the draft package and container labels submitted under amendment 71, dated May 29, 2024.

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 submitted on May 29, 2024. 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 29, 2024, 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/guidancecomplianceregulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125796, 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.
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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). 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 waiving the pediatric study requirement for ages from birth to less than 2 months of age because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group and is not likely to be used in a substantial number of pediatric patients in this group.

We are deferring submission of your pediatric studies for ages 2 months to less than 5 years and 5 years to less than 18 years with certain disease conditions, such as severe asthma, chronic lung disease, cystic fibrosis, congenital heart disease or neuromuscular disorders, for this application because this product is ready for approval for use in individuals 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 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-1345-P101) to evaluate the safety and immunogenicity of MRESVIA in RSV-seropositive children 12 months to < 60 months of age.

   Final Protocol Submission: July 31, 2020

   Study Completion Date: January 31, 2025

   Final Report Submission: December 31, 2025

2. Deferred pediatric study under PREA (mRNA-1365-P101) to evaluate the safety and immunogenicity of MRESVIA in infants and children 5 months to < 24 months of age.

   Final Protocol Submission: December 31, 2022

   Study Completion Date: July 31, 2027

   Final Report Submission: February 28, 2028

3. Deferred pediatric study under PREA (mRNA-1345-P202) to evaluate the safety and immunogenicity of MRESVIA in healthy children 2 years to < 5 years of age,

and children and adolescents at high risk of severe RSV disease 2 years to < 18 years of age.

Final Protocol Submission: September 30, 2023

Study Completion Date: June 30, 2026

Final Report Submission: December 31, 2026

4. Deferred pediatric study under PREA to evaluate the safety and immunogenicity of MRESVIA in infants and children 2 months to < 24 months of age.

   Final Protocol Submission: March 31, 2026

   Study Completion Date: September 30, 2028

   Final Report Submission: March 31, 2029

5. Deferred pediatric study under PREA to evaluate the safety and efficacy of MRESVIA in infants and children 2 months to < 24 months of age.

   Final Protocol Submission: October 31, 2028

   Study Completion Date: May 31, 2031

   Final Report Submission: December 31, 2031

6. Deferred pediatric study under PREA to evaluate the safety and efficacy of MRESVIA in children 2 years to < 5 years of age who are healthy or at risk of severe RSV disease.

   Final Protocol Submission: June 30, 2024

   Study Completion Date: June 30, 2027

   Final Report Submission: December 31, 2027

Submit the protocols to your IND 23342, with a cross-reference letter to this BLA, STN BL 125796, explaining that these protocols were submitted to the IND.

Submit final study reports to this BLA STN BL 125796. 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)**

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 Managers for this application.

Sincerely,

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