



Our STN: BL 125768/0

BLA APPROVAL

August 21, 2023

Pfizer Inc.
Attention: Nirvana Moodley
500 Arcola Road
Collegetown, PA 19426

Dear Ms. Moodley:

Please refer to your Biologics License Application (BLA) received December 21, 2022, submitted under section 351(a) of the Public Health Service Act (PHS Act) for Respiratory Syncytial Virus Vaccine. With the issuance of this approval letter, we have administratively closed BLA STN 125768. Future correspondence and submissions should be addressed to the original BLA STN 125769 for this biological product.

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. 2001. Respiratory Syncytial Virus Vaccine is indicated for active immunization of pregnant individuals at 32 through 36 weeks gestational age for the prevention of lower respiratory tract disease (LRTD) and severe LRTD caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT03529773, NCT04032093, NCT04071158, NCT04424316, and NCT05096208.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Respiratory Syncytial Virus Vaccine. You may label your product with the proprietary name ABRYSSVO. The RSV A and B stabilized prefusion F protein (RSVpreF) drug substances will be manufactured at

(b) (4)

The lyophilized RSVpreF antigen component of the vaccine will be manufactured, filled, and lyophilized at

(b) (4)

. The Sterile Water Diluent Component will be manufactured at

(b) (4)

. The Lyophilized Antigen Component and the Sterile Water Diluent Component to form the final product ABRYSSVO will be labeled and packaged with the vial adapter at

(b) (4)

and at

(b) (4)

The vaccine will be supplied in cartons of 1, 5, and 10 kits, with each kit containing a vial of Lyophilized Antigen Component, a pre-filled syringe containing Sterile Water Diluent Component and a vial adapter.

DATING PERIOD

The dating period for the Lyophilized Antigen Component of Respiratory Syncytial Virus Vaccine shall be 18 months from the date of manufacture when stored at 2-8°C. The dating period for the Sterile Water Diluent Component of Respiratory Syncytial Virus Vaccine shall be 24 months from the date of manufacture when stored at 2-^{(b) (4)}°C. The dates of manufacture shall be defined as the dates of filling into final containers. 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) when stored at (b) (4). The expiration date for the packaged product, Lyophilized Antigen Component with Sterile Water Diluent Component, shall be dependent on the earliest expiration date of either component. Future dating period updates will be submitted as an annual report.

FDA LOT RELEASE

Lot release will occur under BL STN 125769.

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 STN 125769 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 52, dated August 21, 2023, and the draft carton and container labels submitted under amendment 30, dated June 23, 2023.

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 August 21, 2023. 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 June 23, 2023, 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 BL STN 125769 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). In addition to the reporting requirements in 21 CFR 600.80, you must submit adverse experience reports for preterm birth and hypertensive disorders of pregnancy as 15-day expedited reports to the Vaccine Adverse Event Reporting System (VAERS) at <https://vaers.hhs.gov/>. Reports of preterm birth and hypertensive disorders of pregnancy must be submitted as 15-day expedited reports for 3 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 waiving the pediatric study requirement for this indication for ages birth to less than 10 years 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. Conducting clinical studies to evaluate immunization during pregnancy in individuals younger than 10 years of age would not be relevant because of the absence or very limited number of pregnancies in individuals younger than 10 years of age.

We note that you have fulfilled the pediatric study requirement for ages 10 to <17 years for this indication.

We remind you that the requirements for pediatric studies identified in the May 31, 2023, approval letter for STN 125769/0 regarding the indication for individuals 60 years of age and older are postmarketing requirements.

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 a signal of a serious risk of preterm birth, and to identify an unexpected serious risk of hypertensive disorders of pregnancy.

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

Therefore, based on appropriate scientific data, we have determined that you are required to conduct the following studies, in addition to those stated in the May 31, 2023, approval letter for STN 125769:

8. Study titled, “A Rapid Surveillance and Cohort Post-Marketing Safety Study to Evaluate the Safety of Respiratory Syncytial Virus Vaccine (ABRYSVO) Exposure During Pregnancy in the United States” (Protocol C3671027). This postmarketing database study will utilize Sentinel System claims data, including Medicaid claims data, to conduct near real-time monitoring and evaluate preterm birth and hypertensive disorders of pregnancy among approximately 80,000 pregnant women vaccinated with ABRYSVO in the United States compared to a cohort of pregnant women not exposed to ABRYSVO.

We acknowledge the timetable you submitted on August 10, 2023, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: February 29, 2024

Study Completion Date: August 31, 2028

Final Report Submission: February 28, 2029

9. Study titled, “Post-Marketing Safety Study Using a Pregnancy Registry to Evaluate the Safety of Respiratory Syncytial Virus Vaccine (ABRYSVO) Exposure During Pregnancy” (Protocol C3671041). This prospective, non-interventional pregnancy registry will evaluate preterm birth and hypertensive disorders of pregnancy approximately 1,854 pregnant women (including 927 pregnant women exposed to ABRYSVO compared to a group of 927 pregnant women not exposed to ABRYSVO).

We acknowledge the establishment of the contact information for this registry you submitted on August 17, 2023 and the timetable you submitted on August 10, 2023, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: February 29, 2024

Study Completion Date: September 30, 2030

Final Report Submission: September 30, 2031

10. Study titled, “A Post-Marketing Safety Study to Evaluate the Safety of Respiratory Syncytial Virus Vaccine (ABRYSVO) Exposure During Pregnancy in an Integrated Healthcare System in the United States” (Protocol C3671042). This retrospective non-interventional cohort study using electronic healthcare data from a real-world healthcare system in the United States will evaluate preterm birth and hypertensive disorders of pregnancy in at least 4,712 ABRYSVO-exposed pregnant women in comparison to a group of women not exposed to ABRYSVO.

We acknowledge the timetable you submitted on August 10, 2023, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: February 29, 2024

Study Completion Date: February 28, 2029

Final Report Submission: August 31, 2030

11. Study titled, “Safety of respiratory syncytial virus stabilized prefusion F subunit vaccine (RSVpreF) in pregnant women and their offspring in a real world setting in Europe” (Protocol C3671026). This retrospective cohort study using electronic healthcare data from the Vaccine Monitoring Collaboration for Europe (VAC4EU)

will evaluate preterm birth and hypertensive disorders of pregnancy in ABRYSVO-exposed pregnant women compared to pregnant women not exposed to ABRYSVO.

We acknowledge the timetable you submitted on August 10, 2023, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: March 31, 2024

Study Completion Date: March 31, 2029

Final Report Submission: September 30, 2029

Please submit the protocols to your IND 17931, with a cross-reference letter to the BLA, STN BL 125769 explaining that the protocol was submitted to the IND. Please refer to the sequential number for each study and the submission number as shown in this letter.

Please submit the final study reports to the BLA 125769. 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 the BLA, STN BL 125769. For administrative purposes, all submissions related to these postmarketing studies required under section 505(o) must be submitted to the BLA STN BL 125769 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.

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>.

All 15-day alert reports, periodic (including quarterly) adverse drug experience reports, field alerts, PMR/PMC submissions, annual reports, and final study reports should be addressed to BLA STN 125769.

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