Our STN: BL 125769/388 **SUPPLEMENT APPROVAL**

Pfizer Inc. January 6, 2025
Attention: Helen B. Hartman, Ph.D.
500 Arcola Road,
Collegeville, PA 19426

Dear Dr. Hartman:

We have approved your request received November 21, 2024, to supplement your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for Respiratory Syncytial Virus Vaccine (ABRYSVO) manufactured at your Pfizer Manufacturing, (b) (4) facility ((b) (4)), to update the "Warnings and Precautions" and "Adverse Reactions" sections of the Package Insert to include new safety information on the risk of Guillain-Barré syndrome (GBS) following vaccination with ABRYSVO.

The review of this supplement was associated with our October 25, 2024, SAFETY LABELING CHANGE AND POSTMARKETING REQUIREMENT NOTIFICATION LETTER, notifying you, under Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act (FDCA), of new safety information that we believe should be included in the labeling for ABRYSVO. This information pertains to data from a postmarketing observational study that suggest an increased risk of GBS during the 42 days following vaccination with ABRYSVO.

LABELING

We hereby approve the draft content of labeling: Package Insert submitted under amendment 4, dated January 03, 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 submitted on January 03, 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.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 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)).

For each pending supplemental application for this BLA that includes proposed revised labeling, please submit an amendment to update the proposed revised labeling with the changes approved today.

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)).

Since ABRYSVO was approved in 2023, we have become aware of data from a postmarketing observational study conducted among Medicare beneficiaries 65 years of age and older that suggest an increased risk of Guillain-Barré syndrome (GBS) following vaccination with ABRYSVO; please see FDA self-controlled case series GBS update, presented at the October 24, 2024 meeting of the Advisory Committee on Immunization Practices. Therefore, we consider this information to be “new safety information” as defined in section 505-1(b)(3) of the FDCA.

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 serious risk of Guillain-Barré Syndrome following administration of ABRYSVO in pregnant individuals.

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:

1. 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 Guillain-Barré syndrome (GBS) among pregnant women vaccinated with ABRYSVO in the United States.

We acknowledge the timetable you submitted on December 10, 2024, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: June 30, 2025
Study Completion Date: September 30, 2034
Final Report Submission: March 31, 2035

Please submit the protocol to your IND 17931, with a cross-reference letter to BLA STN BL 125769 explaining that this protocol was 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 labeling, the final study report must be submitted as a supplement to BLA STN BL 125769. For administrative purposes, all submissions related to this postmarketing study 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 the approval of BLA STN BL 125769 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.

We will include the information contained in the above-referenced supplement in your BLA file.

Sincerely,

Rebecca Reindel, MD
Director
Division of Clinical and Toxicology Review
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research