Our STN: BL 103914/6290 **SUPPLEMENT APPROVAL**

Sanofi Pasteur Inc.
Attention: Michael Stirr November 4, 2019
Discovery Drive
Swiftwater, PA 18370-0187

Dear Mr. Stirr:

We have approved your request submitted January 4, 2019, received January 4, 2019, to supplement your Biologics License Application (BLA) under section 351(a) of the Public Health Service Act, for Influenza Vaccine (Fluzone®) manufactured at your Swiftwater, PA facility to include the High Dose Quadrivalent formulation for use in persons 65 years of age and older.

The review of this supplement was associated with the following National Clinical Trial (NCT) number: NCT 03282240

LABELING

We hereby approve the draft package insert labeling submitted under amendment 5007, dated October 4, 2019 and the draft carton and container labeling submitted under amendment 5007, dated October 4, 2019.

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. 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 that are identical to the package and container labels submitted on October 4, 2019 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/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications.

All final labeling should be submitted as Product Correspondence to this BLA STN 103914 at the time of use (prior to marketing) 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)).

Please submit an amendment to all pending supplemental applications for this BLA that include revised labeling incorporating a revised content of labeling that includes these changes.

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 birth to less than 6 months of age because the necessary studies are impossible or highly impracticable. This is because we have determined that an immunogenicity study would not be sufficient and that a clinical endpoint efficacy study would be needed. We are deferring submission of your pediatric studies for ages 6 months to < 17 years for this application because the drug or biological product is ready for approval for use in adults 65 years of age and older and 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)(3)(B) 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 the approval of BLA STN 103914/0 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 QHD04 under PREA to evaluate the safety and effectiveness of Fluzone High Dose Quadrivalent, for the prevention of influenza disease caused by influenza subtype A viruses and type B viruses contained in the vaccine in pediatric patients 6 months to <17 years old.

   Final Protocol Submission: September 30, 2018

   Final Study Completion Date: September 30, 2020

   Final Report Submission: April 30, 2021

2. Deferred pediatric study QHD00014 under PREA to evaluate the safety and effectiveness of Fluzone High Dose Quadrivalent, for the prevention of influenza disease caused by influenza subtype A viruses and type B viruses contained in the vaccine in pediatric patients ages 6 months to < 3 years of age.

Final Protocol Submission: September 30, 2021

Study Completion Date: November 30, 2024

Final Report Submission: June 30, 2025

3. Deferred pediatric study QHD00015 under PREA to evaluate the safety and immunogenicity of Fluzone High Dose Quadrivalent, for the prevention of influenza disease caused by influenza subtype A viruses and type B viruses contained in the vaccine in pediatric patients ages 3 to < 5 years.

   Final Protocol Submission: September 30, 2021

   Study Completion Date: June 30, 2023

   Final Report Submission: January 31, 2024

4. Deferred pediatric study QHD00020 under PREA to evaluate the safety and immunogenicity of Fluzone High Dose Quadrivalent, for the prevention of influenza disease caused by influenza subtype A viruses and type B viruses contained in the vaccine in pediatric patients ages 5 to < 9 years.

   Final Protocol Submission: September 30, 2022

   Study Completion Date: June 30, 2024

   Final Report Submission: January 31, 2025

5. Deferred pediatric study QHD00021 under PREA to evaluate the safety and immunogenicity of Fluzone High Dose Quadrivalent, for the prevention of influenza disease caused by influenza subtype A viruses and type B viruses contained in the vaccine in pediatric patients ages 9 to < 18 years.

   Final Protocol Submission: September 30, 2022

   Study Completion Date: June 30, 2024

   Final Report Submission: January 31, 2025

Submit the protocols to your IND 17556, with a cross-reference letter to BLA STN 103914 explaining that these protocols were submitted to the IND.

Submit final study reports to this BLA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated as:

- **Required Pediatric Assessments**

We will include information contained in the above-referenced supplements in your BLA files.

Sincerely,

Doran L. Fink, M.D., Ph.D.
Deputy Director - Clinical
Division of Vaccines and
Related Products Applications
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research