Our STN: BL 125701/0 **BLA APPROVAL**

Sanofi Pasteur, Inc. April 23, 2020
Attention: Michael F. Stirr
Discovery Drive
Swiftwater, PA 18370-0187

Dear Mr. Stirr:

Please refer to your Biologics License Application (BLA) submitted and received on April 26, 2019, under section 351(a) of the Public Health Service Act (PHS Act) for Meningococcal (Groups A, C, Y, W) Conjugate Vaccine.

LICENSING

We have approved your BLA for Meningococcal (Groups A, C, Y, W) Conjugate Vaccine effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Meningococcal (Groups A, C, Y, W) Conjugate Vaccine under your existing Department of Health and Human Services U.S. License No. 1725. Meningococcal (Groups A, C, Y, W) Conjugate Vaccine is indicated for active immunization for the prevention of invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, W, and Y. Meningococcal (Groups A, C, Y, W) Conjugate Vaccine is approved for use in individuals 2 years of age and older.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT02842853, NCT02842866, NCT02199691, NCT02752906, NCT00631995, NCT01732627, and NCT03077438.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Meningococcal (Groups A, C, Y, W) Conjugate Vaccine drug substances at (b) (4) Swiftwater, PA. The final formulated product will be manufactured, filled, labeled and packaged at Swiftwater, PA. You may label your product with the proprietary name MenQuadfi and market it in a 2.0 mL glass vial, in packages of 5 vials.

We did not refer your application to the Vaccines and Related Biological Products Advisory Commitee 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 Meningococcal (Groups A, C, Y, W) Conjugate Vaccine shall be 36 months from the date of manufacture when stored at 2 °C to 8 °C. The date of manufacture shall be defined as the date of final fill 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 each of the four drug substances shall be (b) (4) when stored at (b) (4) .

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, 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

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 Meningococcal (Groups A, C, Y, W) Conjugate Vaccine, or in the manufacturing facilities.

LABELING

We hereby approve the draft package insert labeling submitted under amendment 39, dated April 17, 2020, and the draft carton and container labeling submitted under amendment 38, dated April 14, 2020.

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 April 14, 2020, 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 125701 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)).

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/electronicsubmissionsgateway/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.

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 0 to 6 weeks 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 6 weeks through 23 months of age for this application because this product is ready for approval for use in individuals 2 years of age and older before all pediatric studies have 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 (MET41) under PREA to evaluate the safety of MenQuadfi in infants and toddlers 6 weeks through 12 months of age.

Final Protocol Submission: November 9, 2017

Study Completion Date: August 10, 2022

Final Report Submission: August 31, 2023

2. Deferred pediatric study (MET42) under PREA to evaluate the immunogenicity and safety of MenQuadfi in infants and toddlers 6 weeks through 18 months of age.

   Final Protocol Submission: November 9, 2017

   Study Completion Date: December 15, 2022

   Final Report Submission: July 31, 2024

3. Deferred pediatric study (MET61) under PREA to evaluate the immunogenicity and safety of MenQuadfi in infants and toddlers 6 through 23 months of age.

   Final Protocol Submission: June 22, 2018

   Study Completion Date: August 5, 2022

   Final Report Submission: February 28, 2023

Submit the protocols to your IND 14171, with a cross-reference letter to this BLA 125701 explaining that these protocols were submitted to the IND.

Submit final study reports to this BLA 125701. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated as:

- **Required Pediatric Assessments**

We note that you have fulfilled the pediatric study requirement for ages 2 years to <17 years of age for this application.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitment as described in your letter of April 3, 2020, as outlined below:

4. To establish a pregnancy registry (MEQ00070) for MenQuadfi in the United States to collect and analyze the outcome of exposure to MenQuadfi during pregnancy and monitor for any potential safety signals that may arise in this population in routine public health settings.

Final Protocol Submission: November 30, 2020

Study Completion Date: June 30, 2028

Final Report Submission: June 30, 2029

Please submit the clinical protocol to your IND 14171, and a cross-reference letter to this BLA 125701 explaining that this protocol was submitted to the IND.

If the information in the final study report supports a change in the labeling, 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/GuidanceComplianceRegulatoryInformation/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,

Marion F. Gruber, Ph.D.
Director
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research