



Our STN: BL 125741/0

**BLA APPROVAL**

Merck Sharp & Dohme Corp.  
Attention: Charisse Mandimika, M.D.  
351 N. Sumneytown Pike  
P.O. Box 1000  
UG2D-68  
North Wales, PA 19454

July 16, 2021

Dear Dr. Mandimika:

Please refer to your Biologics License Application (BLA) submitted and received November 17, 2020 under section 351(a) of the Public Health Service Act (PHS Act) for Pneumococcal 15-valent Conjugate Vaccine.

## LICENSING

We have approved your BLA for Pneumococcal 15-valent Conjugate Vaccine effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Pneumococcal 15-valent Conjugate Vaccine under your existing Department of Health and Human Services U.S. License No. 0002. Pneumococcal 15-Valent Conjugate Vaccine is indicated for active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F in adults 18 years of age and older.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT02573181, NCT03480763, NCT03547167, NCT03480802, NCT03950622, NCT03950856, NCT03615482

## MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Pneumococcal 15-valent Conjugate Vaccine pneumococcal polysaccharide serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F at (b) (4)

CRM<sub>197</sub> protein at (b) (4)

; drug substance at (b) (4)

The final formulated product will be manufactured and filled at (b) (4), and labeled and packaged at (b) (4)

You may label your product with the proprietary name VAXNEUVANCE and market it in 1.5 mL glass syringe with a Luer-Lok adapter containing 0.5 mL dose of vaccine.

We did not refer your application to the Vaccines and Related Biological Products Advisory Committee (VRBPAC) 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 Pneumococcal 15-valent Conjugate Vaccine shall be 18 months from the date of manufacture, when stored at 2 to 8 °C. The date of manufacture shall be defined as the date of initiation of final fill of the formulated drug product 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, when stored at (b) (4), shall be (b) (4) for serotypes 3, 4, 14, 22F and 33F; shall be (b) (4) for serotypes 1, 6A, 9V, 18C, and 23F; and shall be (b) (4) for serotypes 5, 6B, 7F, 19A, and 19F.

### **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, 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 Pneumococcal 15-valent Conjugate Vaccine, or in the manufacturing facilities.

## **LABELING**

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.

We hereby approve the draft content of labeling including Package Insert, Patient Package Insert, the draft carton labels submitted under amendment 45 dated July 14, 2021, and the draft container label submitted under amendment 42, dated June 17, 2021.

## **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 and Patient Package Insert submitted on July 14, 2021. 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 labels submitted on July 14, 2021 and container label submitted on June 17, 2021, 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 this BLA, STN BL 125741 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), 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/electronic submissions gateway/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>.

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 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 due to limitations of the neonatal immune response.

We are deferring submission of your pediatric studies for ages 6 weeks through 17 years for this application because this product is ready for approval for use in adults 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 (Study V114-029) to evaluate the safety and immunogenicity of VAXNEUVANCE in healthy infants 6 through 12 weeks of age as a 4-dose schedule (2, 4, 6, and 12 to 15 months of age).

Final Protocol Submission: February 22, 2019

Study Completion Date: December 31, 2021

Final Report Submission: April 30, 2022

2. Deferred pediatric study under PREA (Study V114-024) to evaluate the safety and immunogenicity of VAXNEUVANCE when given as catch-up vaccination in healthy children 7 months through 17 years of age.

Final Protocol Submission: December 5, 2019

Study Completion Date: September 30, 2021

Final Report Submission: December 31, 2021

3. Deferred pediatric study under PREA (Study V114-027) to evaluate the safety and immunogenicity of four-dose schedules of VAXNEUVANCE and Prevnar 13 with doses administered at 2, 4, 6 and 12 to 15 months of age, as compared to mixed schedules which begin with Prevnar 13 and change to VAXNEUVANCE at doses 2, 3 or 4.

Final Protocol Submission: August 16, 2018

Study Completion Date: April 30, 2021

Final Report Submission: July 31, 2021

4. Deferred pediatric study under PREA (Study V114-030) to evaluate the safety and immunogenicity of VAXNEUVANCE in HIV-infected children 6 through 17 years of age.

Final Protocol Submission: December 5, 2019

Study Completion Date: August 31, 2022

Final Report Submission: December 31, 2022

Submit the protocols to your IND 14977 with a cross-reference letter to this BLA STN 125741 explaining that these protocols were submitted to the IND.

Submit final study reports to this BLA STN 125741 as supplements. 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, Taruna Khurana, Ph.D. and Tatiana Claro da Silva, Ph.D.

Sincerely,

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