Our STN: BL 125770/0

BLA APPROVAL
October 20, 2023

Pfizer Ireland Pharmaceuticals
Attention: Gosia Mineo
Pfizer Inc.
1 Pfizer Way 190/004/4405
Pearl River, NY 10965

Dear Ms. Mineo:

Please refer to your Biologics License Application (BLA) received October 21, 2022, submitted under section 351(a) of the Public Health Service Act (PHS Act) for Meningococcal Groups A, B, C, W, and Y Vaccine.

LICENSING

We have approved your BLA for Meningococcal Groups A, B, C, W, and Y Vaccine effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Meningococcal Groups A, B, C, W, and Y Vaccine under your existing Department of Health and Human Services U.S. License No. 2060. Meningococcal Groups A, B, C, W, and Y Vaccine is indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroups A, B, C, W, and Y. Meningococcal Groups A, B, C, W, and Y Vaccine is approved for use in individuals 10 through 25 years of age.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT03135834, NCT04440163 and NCT04440176.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Meningococcal Groups A, B, C, W, and Y Vaccine. You may label your product with the proprietary name PENBRAYA. The lyophilized meningococcal groups A, C, W, and Y polysaccharide tetanus toxoid (TT) conjugate component (Lyophilized MenACWY Component) will be manufactured at (b) (4) (b) (4) Pfizer Ireland Pharmaceuticals, (b) (4) (b) (4) and formulated, filled, and lyophilized at (b) (4) (b) (4) The meningococcal serogroup B factor H binding protein component (MenB Component) will be manufactured at (b) (4) (b) (4) and filled at Pfizer Ireland Pharmaceuticals, (b) (4) The Lyophilized MenACWY Component and the MenB Component will be labeled and

packaged with the vial adapter to form the final product PENBRAYA at (b) (4) (b) (4)

The vaccine will be supplied in cartons of 1, 5, and 10 kits, with each kit containing a vial of Lyophilized MenACWY Component, a pre-filled syringe containing MenB Component, and a vial adapter to provide a single dose of PENBRAYA.

ADVISORY COMMITTEE

We did not refer your application to the Vaccines and Related Biological Products Advisory Committee 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 the Lyophilized MenACWY Component of Meningococcal Groups A, B, C, W, and Y Vaccine shall be 18 months from the date of manufacture when stored at 2-8°C. The dating period for the MenB Component of Meningococcal Groups A, B, C, W, and Y Vaccine shall be 24 months from the date of manufacture when stored at 2-8°C. The dates of manufacture for the Lyophilized MenACWY Component and the MenB Component shall be defined as the dates when filling into final containers is initiated. Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency. The expiration date for the packaged product, Lyophilized MenACWY Component plus MenB Component, shall be dependent on the shortest expiration date of any component.

COMPARABILITY PROTOCOL

This approval includes comparability protocols for the following:

- Preparation, qualification, storage, and shipping of (b) (4) (b) (4)
- Lifetime extension for (b) (4)
- Lifetime extension for (b) (4)
- Lifetime extensions for (b) (4)
- (b) (4)
- (b) (4)

Under 21 CFR 601.12(e), approval of a comparability protocol may justify a reduced reporting category for a particular change. In your annual report (21 CFR 601.12(d)), you should report information confirming that the change(s) meet(s) the requirements specified in your approved comparability protocol. Include the information described in 21 CFR 601.12(d)(3).

FDA LOT RELEASE

Please submit final container samples of the product and each kit component in final containers together with protocols showing results of all applicable tests. Please submit 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, 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 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, B, C, W, and Y Vaccine, or in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including: Package Insert submitted under amendment 45, dated October 18, 2023, and the draft carton and container

labels submitted under amendment 40, dated October 13, 2023 and amendment 34, dated September 8, 2023, respectively.

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 October 18, 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 October 13, 2023, and September 8, 2023, respectively, 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 STN BL 125770 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). 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 infants less than 12 months of age for this application because there is evidence strongly suggesting that the biological product would be unsafe in this pediatric age group. Safety data from a clinical study in infants vaccinated with a reduced dosage Trumenba formulation showed an unacceptably high incidence of fever after a single dose. PENBRAYA contains the same MenB component, in the same quantity, as Trumenba.

We are deferring submission of your pediatric studies for children 1 year to less than 10 years of age 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 B1971067) to evaluate the safety and immunogenicity of MenABCWY in individuals 1 year to <10 years of age.

   Final Protocol Submission: November 30, 2023

   Study Completion Date: November 30, 2026

   Final Report Submission: May 31, 2027

2. Deferred pediatric study under PREA (Study C3511005) to evaluate the safety and immunogenicity of MenABCWY in individuals 1 year to <10 years of age.

   Final Protocol Submission: October 31, 2026

   Study Completion Date: May 31, 2030

   Final Report Submission: November 30, 2030

Submit the protocols to your IND 17319, with a cross-reference letter to this BLA STN BL 125770 explaining that these protocols were submitted to the IND.

Submit final study reports to this BLA STN BL 125770. In order for your PREA PMRs to be considered fulfilled, you must submit and receive approval of either an efficacy or a labeling supplement. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated as:

- **Required Pediatric Assessment(s)**

We note that you have fulfilled the pediatric study requirement for ages 10 years to <18 years of age for this application.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitment as described in amendment 27, dated August 4, 2023, as outlined below:

3. A Pregnancy Registry Study to Evaluate the Safety of PENBRAYA Meningococcal Vaccine Exposure During Pregnancy

   Final Protocol Submission: January 31, 2024

   Study Completion Date: April 30, 2032

   Final Report Submission: April 30, 2033

Please submit clinical protocols to your IND 17319, and a cross-reference letter to this BLA STN BL 125770 explaining that this protocol was submitted to the IND.

If the information in the final study report supports a change in the label, 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 Managers for this application.

Sincerely,

David C. Kaslow, MD
Director
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research