DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ACCELERATED SUPPLEMENT APPROVAL

Our STN: BL **125549/17**

Wyeth Pharmaceuticals, Inc.
Attention: Elisa Harkins
401 N. Middletown Road
Pearl River, NY 10965

April 14, 2016

Dear Ms. Harkins:

We have approved your request to supplement your Biologics License Application (BLA) for Meningococcal Group B Vaccine (Trumenba) manufactured at your [redacted] facility in [redacted], to include a two-dose schedule (a dose administered at 0 and 6 months) according to the regulations for accelerated approval, 21 CFR 601.40-46. Also, we have approved a modification of the three-dose schedule from administration at 0, 2, and 6 months to administration at 0, 1-2, and 6 months.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT01323270, NCT01299480 and NCT01461993.

ACCELERATED APPROVAL REQUIREMENTS

We are granting marketing approval of a two-dose schedule for this product under the accelerated approval of biological products regulations, 21 CFR 601.40-46. Under these regulations, we may grant marketing approval for a biological product on the basis of adequate and well-controlled clinical trials establishing that the biological product has an effect on a surrogate endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. This approval requires you to study the biological product further, to verify and describe its clinical benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to ultimate outcome.

Approval of a two-dose schedule for Trumenba under these regulations requires, among other things, that you conduct adequate and well-controlled studies to verify and describe the clinical benefit of this schedule. Clinical benefit will be confirmed by demonstration of effectiveness against diverse meningococcal group B strains.

ACCELERATED APPROVAL REQUIRED STUDIES

We remind you of your postmarketing requirement specified in your submission of November 25, 2015, and as clarified in your communication dated March 14, 2016.

1. To conduct a study to assess safety, tolerability, and immunogenicity of Trumenba administered on a 0-, 6-month schedule in healthy subjects aged ≥10 to <26 years.

   Final Protocol Submission: June 30, 2016

   Study Completion: August 31, 2019

   Final Report Submission: December 31, 2019

We expect you to complete design, initiation, accrual, completion, and reporting of this study within the framework described in your submission of November 25, 2015.

You must conduct this study with due diligence. If the postmarketing study fails to verify that clinical benefit is conferred by the two-dose schedule, or is not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 601.43 (b), withdraw or modify approval if:

- A postmarketing clinical study fails to verify clinical benefit
- The applicant fails to perform the required postmarketing study with due diligence
- Use after marketing demonstrates that postmarketing restrictions are inadequate to ensure safe use of the biological product
- The applicant fails to adhere to the postmarketing restrictions agreed upon
- The promotional materials are false or misleading
- Other evidence demonstrates that the biological product is not shown to be safe or effective under its conditions of use.

Submit the final study report to this BLA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing study requirement must be clearly designated as **"Subpart E Postmarketing Study Requirements."**

LABELING

Please provide your final content of labeling in Structured Product Labeling (SPL) format and include the carton and container labels. In addition, please submit three original paper copies for carton and container final printed labeling. All final labeling should be submitted as Product Correspondence to this BLA at the time of use (prior to marketing) and include implementation information on FDA Form 356h.

In addition, please submit the final content of labeling (21 CFR 601.14) in 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 titled, *"SPL Standard for Content of Labeling Technical Qs and As"* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

PROMOTIONAL MATERIALS

Please note that the accelerated approval regulation concerning promotional materials (21 CFR 601.45) stipulates that all advertising and promotional labeling items that you wish to distribute in the first 120 days following approval, must have been received by FDA prior to the approval date. After approval, promotional items intended for dissemination after the first 120 days following approval must be submitted to the FDA 30 days prior to the anticipated distribution date. Please submit draft materials with a cover letter noting that the items are for accelerated approval, and an accompanying 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 advertisement and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

Alternatively, you may submit promotional materials for accelerated approval products electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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 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 formulation showed an unacceptably high incidence of fever after a single dose.

We are deferring submission of your pediatric study for children 1 year to less than 10 years of age for this application because the two-dose regimen is ready for approval for use in persons 10 through 25 years of age and the study in children 1 year to less than 10 years of age has not been completed.

Your deferred pediatric study required under 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) is a required postmarketing study. The status of this postmarketing study 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 Requirements/Commitments and submit it to the FDA each year within 60 calendar days of the anniversary date of this BLA this letter until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. This required study and timeline described in your submission of January 15, 2016, are outlined below:

2. A deferred pediatric study under PREA to evaluate the safety and immunogenicity of a 2-dose regimen (0 and 6 months) of Trumenba in children 1 year to less than 10 years of age for the prevention of invasive group B meningococcal disease.

   Final Protocol Submission: May 31, 2018

   Study Completion: December 30, 2020

   Final Report Submission: May 31, 2021

Submit the protocol to your IND 13812, with a cross-reference letter to this BLA 125549 explaining that this protocol was submitted to the IND.

Submit the final study report to this BLA. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated **"Required Pediatric Assessment(s)."**

We will include information contained in the above-referenced supplement in your biologics license application file.

Sincerely yours,

Wellington Sun, M.D.
Director
Division of Vaccines and
Related Products Applications
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research

Attachment: Approved Final Draft Labeling