Our STN: BL 125106/1469 **SUPPLEMENT APPROVAL**

GlaxoSmithKline Biologicals October 7, 2022
Attention: (b) (4)
14200 Shady Grove Road
VR1500
Rockville, MD 20850-7464

Dear Ms. (b) (4):

We have approved your request received on December 15, 2020, to supplement your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed (BOOSTRIX), manufactured at your Rixensart, Belgium facility, to include immunization during the third trimester of pregnancy to prevent pertussis in infants younger than 2 months of age.

The review of this supplement was associated with the following National Clinical Trial (NCT) numbers: NCT02422264 and NCT02853929.

LABELING

We hereby approve the draft content of labeling: Package Insert submitted under amendment 20, dated October 4, 2022.

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 4, 2022. 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.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125106 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)).

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

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 children <10 years of age 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. Conducting clinical studies to evaluate immunization during pregnancy in the age groups 0 to <10 years would not be relevant, taking into consideration the absence or very limited number of pregnancies in individuals younger than 10 years of age and given that routine infant vaccination with Diphtheria and Tetanus Toxoids and Acellular Pertussis (DTaP) vaccines begins at 2 months of age; immunization during pregnancy is intended to prevent pertussis in infants younger than 2 months of age, before they can receive vaccination.

We note that you have fulfilled the pediatric study requirement for ages 10 to 17 years for this application.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitment as described in your correspondence of October 4, 2022, as outlined below:

1. To conduct Study EPI-PERTUSSIS-075 VS US PR, an observational, exposure cohort study to evaluate pregnancy outcomes in individuals exposed to Boostrix as of the 1st day of the 27th week of gestation compared to pregnancy outcomes in individuals who do not receive any Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap) during pregnancy. The registry will continue for at least 4 years, to prospectively collect data on 3000 pregnant individuals, including 1,500 exposed to Boostrix during pregnancy and 1,500 unexposed to any Tdap vaccine throughout pregnancy.

    Final Protocol Submission: January 31, 2023

    Study/Trial Completion Date: December 31, 2026

    Final Report Submission: January 31, 2027

Please submit clinical protocols to your IND 8461, and a cross-reference letter to BLA STN BL 125106 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 Status Update**
- **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 the approval of BLA STN BL 125106/1469 until all requirements and commitments subject to the reporting requirements of section 506B of the Federal Food, Drug, and Cosmetic Act (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.

We will include information contained in the above-referenced supplement in your BLA file.

Sincerely,

For Rebecca Reindel, M.D.
Acting Deputy Director - Clinical
Division of Vaccines and
Related Products Applications
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research