Our STN: BL 125265/645

SUPPLEMENT APPROVAL

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

November 4, 2022

Dear Ms. Mann:

We have approved your request received December 16, 2021, to supplement your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for Rotavirus Vaccine, Live, Oral (ROTARIX) to include a porcine circovirus (PCV)-free liquid formulation of ROTARIX in an oral dosing applicator only presentation, manufactured at your (b)(4), Belgium location, and labeled and packaged at your (b)(4) location, and a squeezable tube presentation, manufactured, labeled and packaged at your (b)(4), Belgium location, for the prevention of rotavirus gastroenteritis caused by G1 and non-G1 types (G3, G4, and G9) in infants 6 weeks and up to 24 weeks of age.

The review of this supplement was associated with the following National Clinical Trial (NCT) numbers: NCT02914184, NCT03207750, and NCT03954743.

DATING PERIOD

The dating period for the oral dosing applicator only presentation of ROTARIX shall be 36 months from the date of manufacture when stored at 2-8°C. The dating period for the squeezable tube presentation of ROTARIX shall be 24 months from the date of manufacture when stored at 2-8°C. The date of manufacture for each of these presentations of ROTARIX shall be defined as the date of filling.

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: Package Inserts submitted under amendment 22, dated October 11, 2022; Patient Package Inserts submitted under amendment 22, dated October 11, 2022; and the draft carton and container labels submitted under amendment 23, dated October 12, 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 and Patient Package Insert, submitted on October 11, 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.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on October 12, 2022, 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/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125265 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 these changes.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitment as described in your correspondence of August 26, 2022, as outlined below:

1. To conduct a prospective observational postmarketing study (study 212329, protocol EPI-ROTA-070 VS LAT) to evaluate intussusception following administration of ROTARIX liquid formulation in Latin America

   Final Protocol Submission: August 31, 2024

   Study/Trial Completion Date: May 31, 2028

   Final Report Submission: July 31, 2028

Please submit clinical protocols to your IND 16992, and a cross-reference letter to BLA STN BL 125265 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 125265 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