Our STN: BL 125510/143

SUPPLEMENT ACCELERATED APPROVAL/ RELEASE PREA PMR

Seqirus, Inc.
Attention: Peggy Charpie, M.S.
50 Hampshire Street, 9th floor
Cambridge, MA 02139

February 21, 2020

Dear Ms. Charpie:

We have approved your request submitted on January 18, 2019, and received on January 22, 2019, to supplement your Biologics License Application (BLA) under section 351(a) of the Public Health Service Act for Influenza Vaccine, Adjuvanted (FLUAD) to include a quadrivalent formulation (FLUAD QUADRIVALENT) manufactured at your Holly Springs, NC facility, for active immunization of persons 65 years of age and older against influenza disease caused by seasonal influenza virus subtypes A and types B contained in the vaccine according to the regulations for accelerated approval, 21 CFR 601.41.

The review of this supplement was associated with the following National Clinical Trial (NCT) numbers: NCT03314662 and NCT02587221.

ACCELERATED APPROVAL REQUIREMENTS

Under accelerated approval 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 under these regulations requires, among other things, that you conduct adequate and well-controlled clinical trials to verify and describe clinical benefit attributable to this product. Clinical benefit is evidenced by effects such as demonstration of efficacy against influenza disease in adults 65 years of age and older.

Accelerated Approval Required Studies

We remind you of your postmarketing requirement specified in your submission of January 10, 2020.

1. To conduct V118_24, a clinical disease endpoint trial in subjects 65 years of age and older with Fluad Quadrivalent.

   Final Protocol Submission: July 31, 2020

   Study/Trial Completion: March 31, 2024

   Final Report Submission: September 30, 2024

We expect you to complete design, initiation, accrual, completion, and reporting of this study within the framework described in your letter of January 10, 2020.

You must conduct this clinical study with due diligence. If the postmarketing study fails to verify that clinical benefit is conferred by Influenza Vaccine, Adjuvanted 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

Please submit the protocol to your IND 15684 with a cross-reference letter to BLA 125510 explaining that this protocol was submitted to the IND. Please refer to the sequential number for each clinical study and the submission number as shown in this letter.

Your accelerated approval postmarketing required study is 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 BLA until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released.

Please submit the final study report as a supplement to BLA 125510. For administrative purposes, all submissions related to this postmarketing study requirement must be clearly designated as “Subpart E Postmarketing Study Requirements.”

LABELING

We hereby approve the draft package insert labeling submitted under amendment 22, dated February 19, 2020, and the draft carton and container labeling submitted under amendments 21 and 16, dated February 14, 2020 and January 10, 2020, 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. 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.

PACKAGE AND CONTAINER LABELS

Please electronically submit final printed package and container labels that are identical to the package and container labels submitted on February 14, 2020 and January 10, 2020, 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/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 125510 at the time of use (prior to marketing) and include implementation information on Form FDA 356h.

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 at least 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)).

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.

RELEASE FROM POSTMARKETING REQUIREMENTS FOR FLUAD

In our November 24, 2015, approval letter for BLA STN 125510/0, we deferred the submission of your pediatric studies for ages 0 to less than 9 years because this product was ready for approval for use in adults 65 years of age and older and the pediatric studies had not been completed.

We have received your amendment submitted on October 29, 2019, and received on October 31, 2019, requesting release from the following pediatric postmarketing requirements (PMRs) identified in the November 24, 2015, approval letter.

PMR # 4. Deferred pediatric trial (V118_19) under PREA to evaluate the safety and immunogenicity of Fluad (aQIV) when administered to children 6 years to less than 9 years of age.

Final Protocol Submission: September 2020

Study Completion Date: May 2022

Final Report Submission: February 2023

We have completed the review of your submission and conclude that you are released from the above PMR for the following reason:

We are waiving the pediatric study requirement for ages 6 years to less than 9 years 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.

PMR # 5. Deferred pediatric trial (V118_14) under PREA to evaluate the safety and immunogenicity of Fluad (aQIV) when administered to infants less than 6 months of age.

Final Protocol Submission: September 2020

Study Completion Date: May 2022

Final Report Submission: February 2023

We have completed the review of your submission and conclude that you are released from the above PMR for the following reason:

We are waiving the pediatric study requirement for ages 0 months to less than 6 months because necessary studies are impossible or highly impracticable. This is because we have determined that an immunogenicity study would not be sufficient and that a clinical endpoint efficacy study would be needed.

The above PMRs are now considered closed.

PEDIATRIC REQUIREMENTS FOR FLUAD QUADRIVALENT

We are waiving the pediatric study requirement for ages 0 months to less than 6 months because necessary studies are impossible or highly impracticable.

We are waiving the pediatric study requirement for ages 6 years to less than 17 years 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.

We are deferring submission of your pediatric study for ages 6 months to less than 72 months for this application because this product is ready for approval for use in adults and the pediatric assessment has not been submitted.

Your deferred pediatric study required under section 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)(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 the approval of BLA 125510 until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. This required study is listed below:

2. Deferred pediatric trial (V118_05) under PREA to evaluate the efficacy, safety and immunogenicity of Fluad (aQIV) when administered to children 6 months to less than 72 months of age.

   Final Protocol Submission: August 2013 (Completed)

   Study Completion Date: July 2018 (Completed)

   Final Report Submission: April 2019 (Submitted)

We have received your submission, submitted and received on March 29, 2019, that includes the final study report for the above PMR. If the information in the final study report supports a change in the labeling, the final study report should be submitted as a supplement to BLA STN 125510. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated as:

- **Required Pediatric Assessment**

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

Sincerely,

Doran L. Fink, M.D., Ph.D.
Deputy Director - Clinical
Division of Vaccines and
Related Products Applications
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research