CBER MEMORANDUM

To: Seqirus

Re: Labeling Supplement to FLUAD and FLUAD Quadrivalent to update Pediatric Use subsection (125510/191)

From: Rachel Zhang, MD
Medical Officer, CRB1/DVPRPA/OVRR/CBER

Through: Maria Allende, MD
Branch Chief, CRB1/DVPRPA/OVRR/CBER

Background

Fluad, an adjuvanted trivalent influenza vaccine, was licensed under accelerated approval on November 24, 2015 (STN 125510/0), with the indication of active immunization against disease caused by influenza virus subtypes A and type B contained in the vaccine in persons 65 years of age and older. Fluad Quadrivalent, an adjuvanted quadrivalent influenza vaccine, was licensed under accelerated approval on February 21, 2020 (STN 125510/0), with the indication of active immunization against disease caused by influenza virus subtypes A and type B contained in the vaccine in persons 65 years of age and older. The sponsor, Seqirus, was granted partial waivers of the pediatric study requirements for Fluad and Fluad Quadrivalent in infants 0 to <6 months of age and in children and adolescents 6 years to <17 years of age. Two deferred pediatric trials (V118_05 and V70_29) in children 6 months to <72 months have been completed. Seqirus has now submitted a labelling supplement to the license application (125510/191) which includes the final study reports for these two studies and updates to the Pediatric Use subsection of the package inserts for Fluad and Fluad Quadrivalent.

Review summary

In the safety and immunogenicity study V70_29, Fluad (aTIV) met the pre-specified noninferiority criteria against Agriflu and Fluzone for all 3 strains contained in the vaccine. In the efficacy study V118_05, Fluad Quadrivalent (aQIV) failed to meet the pre-specified efficacy success criteria to demonstrate relative efficacy (LL of 95% CI of rVE >0%) of aQIV compared to a licensed comparator seasonal influenza vaccine (Fluzone). The majority of influenza cases in the study were A/H3N2 that was not antigenically matched to the strain contained in the vaccine. In this study, aQIV was found to be noninferior compared to the comparator vaccine based on immunogenicity. Solicited adverse reactions were higher in the aTIV and aQIV arms compared to the non-adjuvanted comparator vaccines. No difference in SAEs was observed between the study arms.

Given both studies demonstrated that aTIV/aQIV met immunogenicity criteria for non-inferiority compared to a licensed influenza comparator vaccine, and there were no major safety concerns observed for the use of aTIV/aQIV in this study population, there is insufficient evidence to conclude that the vaccine is unsafe or ineffective. As the efficacy success criterion was not met in study V118_05, there is also insufficient evidence to conclude that the vaccine is effective. The Division determined that the data from these studies could support accelerated approval for the age group 6 to < 72 months. However, the sponsor withdrew a previously submitted efficacy supplement for use in this age group, indicating a company decision to not conduct another pediatric efficacy trial that would be required

under accelerated approval and to not pursue use in this pediatric age group. The Division concludes that the submitted studies provide inconclusive evidence for the effectiveness of this vaccine in the pediatric age group of 6 to < 72 months. However, since the applicant conducted the required PREA studies, the Division concludes that the PREA PMRs are fulfilled.

The review and recommendations were presented to PeRC on October 13, 2020, and PeRC agreed with the Division's conclusions. The revised label containing CBER edits to sections 8.4 were sent to Seqirus and Seqirus agreed to accept all changes.

Label
The following changes were made to the package insert:

FLUAD:
8.4 Pediatric Use
Safety and effectiveness of FLUAD and FLUAD QUADRIVALENT (same manufacturing process and overlapping composition with FLUAD) were evaluated in clinical trials conducted in children 6 months to <72 months of age. Data from these trials are inconclusive to demonstrate the safety and effectiveness of FLUAD in children 6 months to <72 months of age. The safety and effectiveness of FLUAD in infants less than 6 months of age and in children older than 72 months of age have not been evaluated.

FLUAD QUADRIVALENT
8.4 Pediatric Use
Safety and effectiveness of FLUAD and FLUAD QUADRIVALENT were evaluated in clinical trials conducted in children 6 months to <72 months of age. Data from these trials are inconclusive to demonstrate the safety and effectiveness of FLUAD QUADRIVALENT in children 6 months to <72 months of age. The safety and effectiveness of FLUAD QUADRIVALENT in infants less than 6 months of age and in children older than 72 months of age have not been evaluated.

Conclusion:
The final package insert changes in section 8.4 are acceptable. The sponsor has fulfilled the pediatric study requirement for ages 6 months to <72 months for this application.