Application Type	BLA Supplement
STN	125408/127; 125408/127.2 received on 7/20/2015 Amendment 10 received on 1/20/2016
CBER Received Date	April 23, 2015
PDUFA Goal Date	April 25, 2016
Division / Office	DVRPA/OVRR
Clinical Reviewer(s)	Ralph LeBlanc, M.D., Ph.D.
Project Manager	Helen S. Gemignani
Priority Review	No
Reviewer Name(s)	Lihan Yan, Ph.D.
Review Completion Date / Stamped Date	
Supervisory Concurrence	Tsai-Lien Lin, Ph.D., Team Leader A. Dale Horne, Dr. P.H., Branch Chief
Applicant	Novartis Vaccines and Diagnostics, Inc.
Established Name	Flucelvax® Quadrivalent, inactivated subunit-influenza vaccine
(Proposed) Trade Name	Flucelvax® Quadrivalent
Pharmacologic Class	Influenza Vaccine
Formulation(s), including Adjuvants, etc	Suspension for injection supplied in 0.5-mL single-dose pre-filled syringes.
Dosage Form(s) and Route(s) of Administration	H1N1-15 mcg;H3N2-15 mcg;B1-15 mcg; B2-15 mcg/0.5mL; Intramuscular (IM)
Dosing Regimen	One or two doses (at least 4 weeks apart) for persons 4 through 8 years of age depending on vaccination history; one dose for persons 9 years of age and older
Indication(s) and Intended Population(s)	For use in persons 4 years of age or older for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B contained in the vaccine.

SUMMARY

The purpose of this addendum to the statistical review dated January 20, 2016 is to address the Major Amendment (Amendment 10) which the applicant submitted on January 20, 2016. In the submission, the applicant requested approval for an indication in individuals 18 and older for Flucelvax (Quadrivalent) using the current traditional approval process, and licensure for 4 to <18 years of age for Flucelvax (Quadrivalent) using the accelerated approval provisions. This plan is because Flucelvax (Trivalent), the comparator vaccine used to show noninferiority of Flucelvax Quadrivalent, is not yet licensed in the US for use in individuals 4 to < 18 years of age.

The applicant agreed to conduct a confirmatory clinical endpoint study using Flucelvax (Quadrivalent) among subjects 4 to <18 years of age to confirm the clinical benefit of the vaccine, thereby enabling traditional approval of Flucelvax (Quadrivalent). A brief description of the study was provided in the cover letter, and the synopsis of the study (V130_12) was submitted to IND 15744/22 on March 10, 2016.

The evaluation of the immunogenicity results in Study V130_03 among subjects 4 to <18 years of age against the CBER criteria for accelerated approval for influenza vaccines was included in the original statistical review. All CBER criteria were met, therefore supporting accelerated approval of Flucelvax® Quadrivalent in subjects 4 to <18 years of age.

There was no statistical content included in the amendment to the sBLA. Please refer to the clinical reviewer's review on the appropriateness of the proposed general study design. Please also refer to the preliminary statistical review of the synopsis submitted under the IND by Dr. Elizabeth Teeple, dated April 18, 2016.