Our STN: BLA 125692/0

LATE-CYCLE MEETING MEMORANDUM

November 8, 2019

Seqirus, Inc
Attention: Sonja B. Loar, Pharm. D.
50 Hampshire Street
9th Floor
Cambridge, MA 02139

Dear Dr. Loar:

Attached is a copy of the memorandum summarizing your October 9, 2019, Late-Cycle Meeting teleconference with CBER. This memorandum constitutes the official record of the teleconference meeting. If your understanding of the meeting outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER in writing as soon as possible.

Please include a reference to the appropriate Submission Tracking Number (STN) in future submissions related to the subject product.

If you have any questions, please contact the Regulatory Project Managers, CAPT Edward Wolfgang or Dr. Belete Teferedegne, at (301) 796-2640.

Sincerely,

Loris D. McVittie, Ph.D.
Deputy Director - Regulatory
Division of Vaccines and Related Products Applications
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research

Late-Cycle Meeting Summary

Meeting Date and Time: October 9, 2019, 9:00 AM

Meeting Location: Teleconference

Application Number: BLA 125692/0

Product Name: Influenza A (H5N1) Monovalent Vaccine, Adjuvanted

Proposed Indication: For active immunization for the prevention of disease caused by the influenza A virus H5N1 subtype contained in the vaccine. Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted is proposed for use in persons 6 months and older at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine.

Applicant Name: Seqirus, Inc.

Meeting Chair: Brenda Baldwin, Ph.D.

Meeting Recorder: Belete Teferedegne, D.V.M., Ph.D., DABT
CAPT Edward Wolfgang, Ph.D.

Attendees:

CBER

Diane Alexander
Brenda Baldwin, Ph.D.
Suzanne Carter
Denis Cato
Anissa Cheung, M.Sc.
Carmen Collazo, Ph.D.
Obinna Echeozo, Ph.D.
Maryna Eichelberger, Ph.D.
Karen Farizo, M.D.
Doran Fink, M.D., Ph.D.
Varsha Garnepudi, Ph.D.
Laura Gottschalk, Ph.D.
Anthony Hawkins, M.S.
Andrea Hulse, M.D.
Simleen Kaur, M.Sc.
Christopher Jason, M.D.
Xing Li, Ph.D.
Manju Joshi, Ph.D.
Lucia Lee, M.D.
Cynthia Nolletti, M.D.
Loris McVittie, Ph.D.
Anthony Lorenzo, Ph.D.
Nikunji Sharma, Ph.D.
Adamma Mba-Jonas, Ph.D.
Daphne Stewart
Elizabeth Sutkowski, Ph.D.
Belete Teferedegne, D.V.M, Ph.D.
Edward Wolfgang, Ph.D.
Selwyn Wilson David, M.Sc.
Ye Yang, Ph.D.
Jane Woo, M.D.
Zhiping Ye, M.D., Ph.D.
Marina Zaitseva, Ph.D.

Seqirus

Sonja Loar
KD White
Michele Heintz
Eric Blaesing
Jon Kegerise
Jose Van Boxmeer
Eve Versage
Esther Van Twuijver
Matt Hohenboken
Brett Leav
Karen Jourdan-Brown
Natasha Getz
Rachel Loranger
Steve Case
Jessica Gambill
Geremy Knapp
Darren Carter
Logan LeClair
Celene Runham
Keith Kulowicz
Yumi Buckoski
Pam Pollitt

BARDA

Vittoria Ciocce
Joseph Figlio
Xiomi Tong

BACKGROUND

BLA 125692/0 was submitted as a Rolling BLA for Influenza A (H5N1) Monovalent Vaccine, Adjuvanted. The initial submission was dated December 14, 2018, and the final submission was dated February 1, 2019.

Proposed indication: For active immunization for the prevention of disease caused by the influenza A virus H5N1 subtype contained in the vaccine. Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted is proposed for use in persons 6 months and older at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine.

PDUFA goal date: February 1, 2020

In preparation for this meeting, FDA issued the Late-Cycle Meeting Materials on September 27, 2019.

DISCUSSION

1. Discussion of Substantive Review Issues

a. Regulatory

i. Discuss the approval pathway for children 6 months to < 4 years and 4 years to < 17 years.

Meeting Discussion:
Seqirus acknowledged FDA's comment concerning the required confirmatory trials for traditional approval and added that the clinical trials for children 4 years through 17 years of age and 6 months through < 4 years of age were underway. Seqirus stated that they intend to submit the results by mid 2020 and the first quarter of 2021, respectively.

ii. No discussion at this time on the proposed indication, review of the Prescribing Information (PI) or waiver request for Drug Supply Chain Security Act requirement.

Meeting Discussion:
FDA explained that review of the prescribing information and submitted waiver request for the Drug Supply Chain Security Act requirement is ongoing. Seqirus acknowledged.

b. Pharmacovigilance
We would like to discuss with you the feasibility of conducting, as a postmarketing commitment, a pregnancy registry (see 1(b)(i) above) to actively collect information on cases in which women are exposed to the Influenza A (H5N1) Monovalent Vaccine, Adjuvanted, during pregnancy and the subsequent pregnancy outcomes.

Meeting Discussion:
Seqirus expressed concern over the challenges with establishing a pregnancy registry. These include difficulties in setting up relationships with medical facilities/doctors, difficulties with not being in charge of the distribution and tracking of the vaccine during a pandemic which will be managed by the CDC, and the potential for subjects to receive a pandemic vaccine of a different type/made by a different manufacturer for their second dose administration. CBER recognized the difficulties and offered to have future discussions on this issue. CBER also noted that if the product is approved, the PMC discussion in the approval letter would be at a high level. A suggestion was made by the sponsor to include BARDA, CDC, and Seqirus in the proposed discussions with the FDA.

c. CMC

i. Discuss the appearance of (b) (4) in all (b) (4) BLA batches of (b) (4) of aH5N1c (b) (4) as requested by Seqirus in the amendment dated September 26, 2019.

Meeting Discussion:
Seqirus explained that they implemented experiments to identify the source of the intrensic nature of the (b) (4). In their view of the

issues regarding the (b) (4) observed in filled aH5N1c (b) (4) 6- and 9-month stability samples, Seqirus has concluded that there was an interaction between the product matrix and the stopper material. However, it is unknown if these (b) (4) may effect the quality/potency/safety of the vaccine. FDA acknowledged the investigation undertaken by Seqirus and since the investigations are not final, to submit Seqirus' overall investigation conclusion to FDA when completed.

Seqirus indicated that following the discovery of these (b) (4) and the possible issues this may have on licensure of the aH5N1c vaccine they internally determined to either (b) (4) the vaccine was allowed to be (b) (4) or withdraw the (b) (4) from consideration in the BLA. Ultimately, Seqirus decided to withdraw the (b) (4) vaccine from the BLA application until they can fully address the (b) (4) concern.

ii. We request that you provide an update on the status of providing data on the (b) (4) study, the validation report for the improved method of measuring the kinetics of virus inactivation, and stability data on specific batches indicated in the introduction above.

Meeting Discussion:
Seqirus indicated that since the (b) (4) will be removed from consideration in the BLA, the discussion on stability would only be in regards to the PFS presentation. Seqirus explained that they made a decision to provide only 12-months of stability data (already submitted) instead of the (b) (4) month stability data planned for the BLA. Seqirus (b) (4) month stability data to support an (b) (4) month shelf-life. FDA acknowledged. Seqirus added that since the (b) (4) study results only concern the (b) (4) the (b) (4) information requested by FDA need not be submitted as this presentation is no longer being considered. Seqirus also noted that the validation report for kinetics of virus inactivation was submitted in a recent amendment to the BLA. FDA indicated it still is being reviewed.

2. Outstanding Information Requests (IRs)

IR sent on 9/25/19 regarding Seqirus' proposed pharmacovigilance plan; request for a waiver under 21 CFR 600.90 (a)(1) from reporting requirements under 21 CFR 600.80 and 21 CFR 600.81 until the vaccine is distributed; request for total protein lot results; and Lot Release Protocol (LRP) template.

Meeting Discussion:
Seqirus noted that the responses to the IR from September 25, 2019, were provided recently. FDA indicated that an additional IR was sent on

September 30, 2019 regarding the DSCSA waiver request and October 8, 2019, regarding the (b) (4) . Seqirus acknowledged FDAs additional IRs and indicated they would respond shortly.

3. Risk Management Actions

There is no anticipation of a REMS at this time.

Meeting Discussion:
Seqirus acknowledged.

4. Postmarketing Requirements/Postmarketing Commitments

a. PMR to study safety and immunogenicity of Influenza A (H5N1) Monovalent Vaccine, Adjuvanted, in infants 0 to < 6 months at the time a pandemic is declared.

Meeting Discussion:
Seqirus agreed to the PMR.

b. PMR to confirm clinical disease endpoint efficacy of Flucelvax in children 6 months through < 4 years and 4 years through < 17 years.

Meeting Discussion:
Seqirus agreed to the PMR.

c. PMC to establish a pregnancy registry to prospectively collect data on spontaneously reported exposures to Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted in pregnant women, including data on pregnancy outcomes.

Meeting Discussion:
See discussion 1b above.

5. Major labeling issues

There are no issues identified at this time.

Meeting Discussion:
Seqirus acknowledged.

6. Review Plans

a. The Package Insert and other labeling are under review, and the target date for sending labeling comments to Seqirus is no later than January 2, 2020.

Meeting Discussion:
Seqirus acknowledged.

b. CBER will take an action on this application no later than January 31, 2020.

Meeting Discussion:
Seqirus acknowledged.

7. Applicant Questions

Meeting Discussion:
Seqirus asked if the IR response regarding issues related the (b) (4) formulations, dated September 25, 2019, can be sent to the IND. CBER agreed.

8. Wrap-up and Action Items

a. Arrange a follow up teleconference to discuss and address the challenges of establishing a pregnancy registry.

b. CBER stated the Late Cycle meeting summary will be sent to Seqirus within 30 days.

This application has not yet been fully reviewed by the signatory authorities, Division Directors and Review Committee Chair, and therefore this meeting did not address the final regulatory decision for the application.