Our STN: BLA 125692/0

MID-CYCLE COMMUNICATION SUMMARY

August 9, 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 summary of your July 29, 2019, Mid-Cycle Communication Teleconference with CBER. This memorandum constitutes the official record of the Teleconference. If your understanding of the Teleconference outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER as soon as possible.

Please include a reference to STN 125692/0 in your future submissions related to Influenza A (H5N1) Monovalent Vaccine, Adjuvanted.

If you have any questions, please contact 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 (CBER)

Mid-Cycle Communication Teleconference Summary

Application number:	BLA 125692/0
Product name:	Influenza A (H5N1) Monovalent Vaccine, Adjuvanted (aH5N1c)
Proposed Indication:	For active immunization for the prevention of disease caused by the influenza A virus H5N1 subtype contained in the vaccine in persons 6 months and older at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine.
Applicant:	Seqirus, Inc.
Meeting date & time:	July 29, 2019, 11:00 AM
Committee Chair:	Brenda Baldwin, Ph.D.
RPMs:	Belete Teferedegne, D.V.M., Ph.D., DABT CAPT Edward Wolfgang, Ph.D.

Attendees:

CBER

Brenda Baldwin, Ph.D.
Denis Cato, Ph.D.
Anissa Cheung, M.Sc..
Carmen Collazo, Ph.D.
Selwyn Wilson David, Ph.D.
Obinna Echeozo, Ph.D.
Maryna Eichelberger, Ph.D.
Doran Fink, M.D., Ph.D.
Varsha Garnepudi, M.Sc.
Stuart Hibbs, Ph.D.
Manju Joshi, Ph.D.
Simleen Kaur, M.Sc.
Xing Li, Ph.D.
Cynthia Nolletti, M.D.
Sonny Saini, PharmD
Elizabeth Sutkowski, Ph.D.
Belete Teferedegne, D.V.M, Ph.D.
Edward Wolfgang, Ph.D.
Ye Yang, Ph.D.
Zhiping Ye, M.D., Ph.D.
Iryna Zubkova, Ph.D.

Seqirus

Eric Blaesing
Shannon Harris
Matt Hohenboken
Leah Isakov
Geremy Knapp
Sonja Loar
Laura Matulevich
Celene Runham
Petra Smith
Richard Steere
Liz Strickland
Wendy Su
Patrick Thompson
Eve Versage
K D White

BARDA

Xiaomi Tong

Agenda:

1. **Any significant issues/major deficiencies identified by the Review Committee to date.**

   a. **Product:**

      i. An improved method with a sensitive measure of virus infectivity to demonstrate H5N1 virus inactivation kinetics is required prior to the approval of this BLA application. The validation report of this improved method is not expected to be received by CBER until October 2019.

         ***Discussion*:** Seqirus confirmed that the improved method validation report will be submitted to CBER in early October 2019.

      ii. The specifications for (b) (4) drug substance (DS) release test and the (b) (4) have yet to be updated in Module 3.2.S.4.1.

         Discussion: Seqirus explained that this requested information will be provided in the August 2, 2019, submission along with their response to CBER's Information Request (IR) dated July 19, 2019.

      iii. The potency assay for the adjuvanted drug product includes an (b) (4) . Based on the analytical procedure you submitted, you have not specified the criteria in which this (b) (4) will be executed. In addition, there is inadequate measure to control this (b) (4) to ensure the HA potency is accurately determined.

         Discussion: Seqirus acknowledged CBER's concerns and noted that the potency assay with the (b) (4) was performed with the (b) (4) of HA. Seqirus stated that this information will be provided in the August 2, 2019, submission.

      iv. The (b) (4) study for the aH5N1c (b) (4) final container is ongoing. Data from the accelerated aging and real-time 6-month, 12-month, (b) (4) time points have not been submitted.

         ***Discussion*:** Seqirus indicated that they would have the 6 and 12 month results for the (b) (4) study by January 2020. CBER stated that since the action due date of this BLA was in January of 2020, the proposed submission date would be too late. As the samples will be pulled for analysis in October 2019, CBER asked Seqirus if they would be able to get the results to us by the end of November/early December 2019. Seqirus said that they will reach out to their vendor to request the study data

earlier and will update CBER following vendor discussions regarding their ability to provide the results by the timeframe requested.

v. Stability analyses for (b) (4) batches (b) (4) manufactured with Process 3.0 and Drug Product (DP) PFS batch (b) (4) and (b) (4) batches (b) (4) manufactured using Process 3 are ongoing. The accelerated stability data at 6 months for the DP (b) (4) lots have not been submitted. Additionally, the real time stability data at (b) (4) months for the (b) (4), 6, 9, 12, (b) (4) months for the DP (b) (4) and 12, (b) (4) months for the DP PFS have not been submitted.

***Discussion*:** Seqirus explained they they have (b) (4) months real time (b) (4) stability data, 6 months accelerated and 12 months real time PFS DP stability data, and 6 months accelerated and up to 9 months real time (b) (4) DP stability data currently available and this information will be submitted in the August 2, 2019, submission. Seqirus indicated that additional stability data (i.e., 12 months real time for (b) (4) DP and (b) (4) months real time for PFS DP) would be available for submission to CBER late in December 2019/early January 2020. CBER voiced concern that the additional stability data would be submitted too close to the action due date and requested that Seqirus make a strong effort to submit the data sooner, preferably early December 2019. CBER also stated that the shelf life of these products would be determined by the stability data submitted to the BLA.

vi. Sterility test qualification on drug product (b) (4) using (b) (4) has not been received to date.

Discussion: Seqirus explained that the requested information will be provided in the August 2, 2019, submission.

2. **Information regarding major safety concerns.**
   None identified thus far.

   ***Discussion*:** Seqirus acknowledged the information.

3. **Preliminary Review Committee thinking regarding risk management.**
   CBER continues to conduct a benefit-risk assessment for administering Influenza A (H5N1) Monovalent Vaccine, Adjuvanted in the event of pandemic.

   ***Discussion*:** Seqirus acknowledged the information.

4. **Any information requests sent, and responses not received**.
   IR sent on 7/19/19 with a request that a response be provided to CBER by August 2, 2019.

***Discussion*:** CBER mentioned that an IR regarding subpopulation analyses was emailed to Seqirus on July 24, 2019. Seqirus acknowledged receipt of the IR.

5. **Any new information requests to be communicated.**
   None at this time.

6. **Proposed date(s) for the Late-Cycle Meeting (LCM).**

   a. The LCM between Seqirus and the Review Committee is currently scheduled for October 9, 2019, at 9:00 AM.

   b. We intend to send the LCM materials to Seqirus by September 27, 2019.

   c. If these timelines change, we will communicate updates to you during the course of the review.

   ***Discussion*:** Seqirus acknowledged the LCM information and indicated the date/time should be acceptable.

7. **Updates regarding plans for the AC meeting.**
   CBER does not plan to convene an AC meeting.

   ***Discussion*:** None

8. **Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates.**

   a. Proposed labeling comments: January 2, 2020

   b. Proposed PMC/PMR (if any): January 2, 2020

   c. First Action Due: January 31, 2020

   ***Discussion*:** Seqirus acknowledged the projected milestones.

Additional Discussion: Seqirus indicated that they may try to submit a new proposed proprietary name for review.