



Our STN: BL 125777/0

**MID-CYCLE COMMUNICATION
SUMMARY**

Valneva Austria GmbH
Attention: John Kanaras
Valneva USA, Inc.
910 Clopper Road, Suite 160S
Gaithersburg, MD 20878

May 17, 2023

Dear Mr. Kanaras:

Attached is a copy of the summary of your April 17, 2023, 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 125777/0 in your future submissions related to IXCHIQ.

If you have any questions, please contact the Regulatory Project Managers, Konstantin Virnik, Ph.D. (Konstantin.Virnik@fda.hhs.gov) and Georgeta Crivat, Ph.D. (Georgeta.Crivat@fda.hhs.gov), by email or at (301) 796-2640.

Sincerely,

Loris 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

Mid-Cycle Communication Teleconference Summary

Application Type and Number: BLA 125777/0
Product Name: Chikungunya Vaccine, Live (IXCHIQ)
Proposed Indication for Use: Active immunization for the prevention of disease caused by Chikungunya virus in individuals 18 years and older
Applicant: Valneva Austria GmbH
Meeting Date & Time: April 17, 2023; 12:00 PM-1:30 PM EDT
Committee Chair: Sudhakar Agnihothram, PhD
RPMs: Konstantin Virnik, PhD
Georgeta Crivat, PhD

CBER Attendees:

Sudhakar Agnihothram, Georgeta Crivat, Konstantin Virnik, Sixun Yang, Jana Highsmith, Daphne Stewart, Swati Verma, Kerry Welsh, Peter Weina, Kirk Prutzman, Joseph Toerner, Marisabel Rodriguez, Lisa Stockbridge, Timothy Fritz, John Scott, Diane Gubernot, Loris McVittie, Tony Wang, Ho-Hsiang Wu, Derek Ahneman, Muhammad Shahabuddin, David Rouse, Maria Bagh, Nicolette Devore, Shufeng Liu, Triet Tran, Peter Marks, Lei Huang, Oluchi Elekwachi, Jennifer Kirk, Alicia Howard, Tao Pan, Ching Yim-Banzuelo, David Kaslow, Sara Gagneten, Meghna Alimchandani, Varsha Garnepudi, Andrea Hulse, Marian Major, Rakesh Pandey, Maryna Eichelberger, Andrea Gray, Narayan Nair, Douglas Pratt, Ruoxuan Xiang, Carrie Mampilly, David Cho, Theresa Finn, Cassandra Overking, Brenda Baldwin, Anthony Lorenzo, Martin Green, Dennis Cato, Tsai-Lien Lin, Hector Izurieta

Valneva Attendees:

Juan Carlos Jaramillo, Katrin Dubischar, Susanne Eder-Lingelbach, Vera Bürger, Romana Hochreiter, Karen Lingnau, Klaus Hutter, Zsuzsanna Unger, Shailesh Dewasthaly, Gabriele Fabini.

Discussion Summary

1. Any significant issues/major deficiencies, categorized by discipline, identified by the Review Committee to date:

CBER stated that the protocol for proposed test-negative observational post-marketing confirmatory clinical study (b) (4) -402, titled, “Effectiveness of (b) (4) vaccine against Chikungunya virus disease in the adolescent and adult population in endemic areas of Brazil”, is under review. (b) (5) related to this protocol and requested that Valneva work with CBER to provide timely responses to have an agreed-upon

final protocol prior to a regulatory action on this BLA. On a related note, CBER questioned whether the proposed comparability study of (b) (4) Vs VLA 1553, would be conducted under IND 17854. Valneva confirmed that the comparability study of (b) (4) vs VLA1553 would be performed under IND 17854.

2. Information regarding major safety concerns:

CBER indicated that the review of the safety issues including but not limited to arthralgia/arthritis, spontaneous abortions, neutropenia, and leukopenia was ongoing, and CBER would reach out if additional information was needed.

3. Preliminary Review Committee thinking regarding risk management:

CBER stated that the review of the safety data and pharmacovigilance plan was ongoing, and CBER would provide pharmacovigilance recommendations at a later date.

4. Any information requests sent, and responses not received.

CBER noted that the following information requests are outstanding:

Information request #25 regarding datasets (submitted on March 28, 2023, response to part 2 of the request is pending).

Information request #26 regarding carton and container labels (submitted on April 5, 2023, response expected by April 19, 2023).

Information request #27 regarding CMC (DS testing and DP PPQ) (submitted on April 7, 2023, response expected by April 20, 2023).

Information request #28 regarding endotoxin testing method (submitted on April 10, 2023, response expected by April 17, 2023).

Information request #29 regarding CMC (b) (4) validation and DP control SOP) (submitted on April 13, 2023, response expected by April 20, 2023).

In addition, CBER noted that several new information requests were sent since the agenda had been communicated to Valneva.

5. Any new information requests to be communicated:

CBER stated that information requests regarding samples and reagents for lot release tests, and a pregnancy study proposal (request for a concept protocol) would be communicated in the forthcoming weeks.

6. Proposed date for the Late-Cycle meeting (LCM):

CBER noted that the LCM between Valneva and the Review Committee was currently scheduled for June 22, 2023, 11:30 AM-1:00 PM EDT, and CBER intended to send the LCM materials to Valneva approximately 10 calendar days in advance of the LCM. Any timeline changes will be communicated to Valneva. Valneva pointed out that the LCM date would interfere with the June 21-22 ACIP meeting and asked CBER to reschedule the LCM. CBER acknowledged this and agreed to reschedule the meeting.

7. Updates regarding plans for the AC meeting:

CBER noted that this BLA was not going to be discussed at an Advisory Committee Meeting. Valneva acknowledged this statement.

8. Other projected milestone dates for the remainder of the review cycle:

CBER confirmed the following milestones with Valneva. It was noted that these dates might change if a major amendment notification is issued, and Valneva would be notified of any updates.

Finalized Lot Release Protocol:	by July 23, 2023
Labeling Comments to Applicant:	by July 23, 2023
Notification of PMC/PMR:	by July 23, 2023
Action Due Date (ADD):	August 22, 2023

Other points of discussion:

- Valneva enquired about the lot release testing. CBER briefly described the general process for lot release in-support testing and noted that an information request for samples and reagents for in-support testing would be sent relatively soon. Valneva asked if FDA could specify which assay would be set up and verified by FDA for lot release testing. CBER indicated that neither the tests nor results of these tests could be disclosed, but CBER would notify Valneva about completion of the tests. CBER informed Valneva that if there were any lots pending for release at the time of BLA approval, Valneva should notify FDA in advance. Valneva indicated that they were planning to release launch lots and asked FDA about information that would be necessary at that time. CBER informed Valneva that they should provide lot release protocol 2 weeks prior to ADD. Valneva agreed and informed that they would notify FDA about number of vials to be shipped after the approval of the BLA.
- Valneva inquired whether it was possible to obtain early feedback from FDA regarding container and package labeling. CBER responded that these items would be discussed at the end of April or beginning of May and feedback would be communicated to the company when available.
- Valneva submitted several pre-meeting questions that were discussed at this meeting:

- 1) Question regarding shelf life/ EOS specifications: Can the agency share their view towards 24 months at this stage, following our IR8&IR16 responses?

CBER responded that the agency agreed with the specified shelf life of the DP.

- 2) Question regarding lot release testing at CBER: Can agency share their current thinking on assays to be implemented by CBER?

CBER stated that the response to this question was provided earlier in the discussion.

- 3) Question regarding any clinical trial site inspections.

CBER responded that clinical trial site inspections were being planned and the agency would inform the selected clinical sites about the upcoming inspections.

- 4) Question regarding “other (major) issues identified that we can start addressing now?”

CBER responded that the agency had already informed Valneva about currently identified issues and would communicate any issues identified in the future via information requests.

The meeting concluded at 12:38 PM EDT.