



Our STN: BL 125777/0

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

**LATE-CYCLE
MEETING MEMORANDUM**
July 21, 2023

Dear Mr. Kanaras:

Attached is a copy of the memorandum summarizing your June 23, 2023, Late-Cycle 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 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, 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

Late-Cycle Meeting Summary

Meeting Date and Time: June 23, 2023, 3:00 PM-4:30 PM ET
Meeting Location: Teleconference

Application Number: BLA 125777/0
Product Name: Chikungunya Vaccine, Live (IXCHIQ)
Proposed Indication: Active immunization for the prevention of disease caused by Chikungunya virus in individuals 18 years and older

Applicant Name: Valneva Austria GmbH
Meeting Chair: Sudhakar Agnihothram, PhD
Meeting Recorder: Georgeta Crivat, PhD

CBER Attendees:

Sudhakar Agnihothram, Georgeta Crivat, Marian Major, Swati Verma, Shufeng Liu, Narayan Nair, Kerry Welsh, Joseph Quander III, Hector Izurieta, Christine Harman, Tony Wang, Oluchi Elekwachi, Timothy Fritz, Richard Forshee, Marisabel Rodriguez, Carolyn Renshaw, Cassandra Overking, Alicia Howard, Andrea Gray, Tran Triet, Sixun Yang, Nicolette Devore, Rakesh Pandey, Loris McVittie, Jana Highsmith, David Kaslow, Jennifer Kirk, Lisa Stockbridge, Karla Garcia, Peter Weina, Kirk Prutzman, Lei Huang, Ruoxuan Xiang, Hussein Ezzeldin, Muhammad Shahabuddin, Viviana Ramirez, Tao Pan, Megha Alimchandani, David Rouse, Nicole Trudel, Leyla Beshir, Douglas R. Pratt, Tsai-Lien Lin, Ho-Hsiang Wu, Ching-Long Sun, Linda Forsyth, Carrie Mampilly.

Valneva Attendees:

Juan Carlos Jaramillo, Katrin Dubischar, Susanne Eder-Lingelbach, Vera Bürger, Romana Hochreiter, Karen Lingnau, Klaus Hutter, Shailesh Dewasthaly, Joanna Hope, Gabriele Fabini, Manfred Berger, Krzysztof Rowinski.

Discussion Summary

1. Discussion of Substantive Review Issues

CBER stated that there were two substantive review issues:

- Confirming the effectiveness of IXCHIQ- Observational study protocol (b) (4) 402 [Information Request (IR) #50].

CBER confirmed that they had received responses to IR #50, which were under review, and that they plan on communicating any comments once the review is complete. CBER requested that Valneva work with CBER in a timely manner on finalizing the protocol for (b) (4) -402 prior to the action due date. Valneva inquired about the reason for CBER requesting a second post marketing

effectiveness study, as noted in IR #50. CBER responded that this question was out of scope for discussion at the meeting.

- Shipping Validation Data: CBER requested that Valneva provide a response to IR #55 by the requested date. Valneva responded that they would provide a response to IR #55 by the requested date.

2. Information Requests:

CBER noted that the following information requests are outstanding:

- IR #33: Lot Release: Samples and Reagents-Vero (b) (4) vials have not been delivered to CBER. Valneva noted that vials would be shipped out on June 26, 2023.
- IR #46: Postmarketing Pregnancy Study (response expected by June 16, 2023)- Responses received and are under review.
- IR #48: CMC: (b) (4) validation (response expected by June 16, 2023)- Responses received and are under review.
- IR #50: Postmarketing confirmatory study (b) (4) -402 (response expected by June 16)- Responses received and are under review.
- IR #22: Requalification data with unfiltered viral harvest samples for the mycoplasma method requested by DVP on March 23, 2023 (expected by end of June - mid-July) -Partial response received and under review. A complete response will be submitted by 14 July 2023.
- IR #55: Shipping Validation Studies/Protocol: Discussed under Item #1.

3. Discussion of Upcoming Advisory Committee Meeting

CBER noted that the advisory committee meeting has not been planned.

4. Risk Management Actions (e.g., REMS, the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk)

CBER informed Valneva that issues related to risk management have not been identified and that there was no anticipation of a REMS at this time.

5. Postmarketing Requirements/Postmarketing Commitments

- CBER informed Valneva that details on Post Marketing Requirements (PMRs) and Post Marketing Commitments (PMCs) would be communicated by July 23, 2023.

- Valneva inquired whether CBER could elaborate on the details regarding PMRs and PMCs. CBER responded that there was no additional information to be shared at this time.

6. Major Labeling Issues:

CBER informed Valneva that there were no major labeling issues identified at this time. The package insert, carton and container labels were being reviewed. Our labeling comments would be provided to the sponsor no later than July 23, 2023.

7. Review Plans:

- CBER informed Valneva that the review of their application was currently ongoing. Provided no major review issues arise, CBER intends to take action on this application no later than August 22, 2023.
- Valneva inquired whether this timeline would be maintained and if not, whether possible extensions could be foreseen. CBER responded that it was premature to comment on it, since the application is still under review.

8. Applicant Questions:

Valneva submitted several pre-meeting questions that were discussed at this meeting:

Labelling

Question #1:

Question regarding labelling: Would it be acceptable to initiate printing of the Syringe Container label (Sterile Water Diluent Component) now to allow for a swift launch after licensure?

CBER Response to Question #1:

CBER acknowledged Valneva's response to information request #44, submitted in amendment #45, received on May 30, 2023, that included the revised container label for the sterile water diluent component. Valneva was advised that the revised container label was still under review, and CBER would provide responses once the review was completed. CBER recognized Valneva's need for a timely response and would try to respond in a timely manner. CBER also acknowledged that the request for a linear barcode exemption (21 CFR 201.25) was under review and CBER would reach out with a related IR. Valneva further asked whether CBER could opine on approving the labels. CBER responded that approval of the labels is tied to the final regulatory action on the BLA. While CBER may be able to provide their assessment of whether they have any further comments on the labels, it would be up to Valneva to decide whether to print the labels at risk pending final approval of the BLA.

Question #2:

Question regarding proposed NDC code for the final product as 42515-003-01: Can the agency confirm the acceptability of the NDC code as it is required to set up the serialization and other systems in the product logistics?

CBER Response to Question #2:

CBER acknowledged submission of the proposed NDC code of the final product as 42515-003-01, received in amendment #3, dated December 22, 2022. For securing NDCs, Valneva should contact the eDRLS staff at edrls@fda.hhs.gov. CBER clarified that the NDC Reservation submission is not a drug listing submission, but it serves as a tool for a sponsor to secure an NDC for drugs awaiting approval.

Promotional Materials submission

Question #3:

Question regarding Promotional Materials submission: Valneva plans to submit to APLB/FDA promotional materials to be used within 120 days of approval. Currently we estimate ~40 pieces (Launch Materials) to be used in the initial 120 days of approval. We propose to submit ~4 Core promotional pieces 1st week in August (after the comments from PI are received) for active review by APLB. The remaining materials are planned to be derivatives of the 'approved' Core pieces. The derivative pieces will be submitted to FDA at the time of initial dissemination (Form 2253 submissions). Does the agency agree to the approach?

CBER Response to Question #3:

CBER stated that they did not agree with the proposal regarding submission of promotional materials since it does not comply with the regulations and the current guidance. Valneva should contact FDA/ Advertising, Promotional and Labeling branch, Dr. Lisa Stockbridge, email: Lisa.Stockbridge@fda.hhs.gov for details on how to provide CBER with the presubmission of their promotional materials for the first 120 days after approval, as well as the presubmission requirements for all promotional materials thereafter.

CMC

Question #4:

Does FDA agree to the use of CHIKV Drug Product batch (b) (4) for commercial launch in absence of (b) (4) of (b) (4) ?

Does FDA agree to the use of all other (b) (4) batches produced in the PPQ campaign for future commercial batches?

CBER Response to Question #4:

CBER agreed that CHIKV Drug Product batch (b) (4) could be used for commercial launch and that all other (b) (4) batches produced in the PPQ campaign could be used for future commercial batches.

Question #5:

Valneva provided three Drug Product batches for the set-up of the analytical methods at CBER, including batch (b) (4), which is planned to be used for commercial launch (please refer to response to #IR33 and Question #4 above).

Samples from our proposed launch batch (b) (4) were provided to CBER. Does the FDA foresee a need for additional samples for lot release for this batch?

CBER Response to Question #5:

CBER said that they did not need additional samples for lot release of batch (b) (4). Valneva should submit the Lot Release Protocol for this lot to the Product Release Branch, Office of Compliance and Biologics Quality, when complete. For additional information, Valneva could contact Joseph Quander III, Chief PRB at Joseph.Quander@fda.hhs.gov and their centralized email account CBERLotRelease@fda.hhs.gov

Drug Product Shipment Validation Status

Question # 6:

Shipment Validation for the Drug Product Lyophilized and Sterile Water for Injection has been completed. Shipment Validation for the Final Product (commercial kit) (including Essential Performance Requirement (ERP) evaluation) and (b) (4) testing is ongoing. An overview of the shipment validations is provided in the table below. All reports will be provided to FDA by end August 2023, prior to shipment of the initial product to the USA.

Shipment Validation	Protocol	Report	Status	Comments
Drug Product Lyophilized	VIE-VP-0218 (3.2.P.3.5- Appendix 12)	VIE-VR-0230 (3.2.P.3.5- Appendix 12)	Complete	VIE-VR-0230 provided in Sequence 38
Sterile Water for Injection (sWFI)	VIE-VP-0216 (3.2.P.3.5- Appendix 13)	VIE-VR-0229 (3.2.P.3.5- Appendix 13)	Complete	VIE-VR-0229 provided in Sequence 38

Finished Product (Mock Product, Commercial Kit), Road/Air for Europe and US (b) (4)	VIE-VP-0217 (3.2.P.3.5-Appendix 14)	VIE-VR-0232 (VLA1553 Final Product Road Shipping Validation Report)	Ongoing	Reports will be submitted by 21 July 2023
	VIE-VP-0227 (VLA1553 Air Shipping Validation Protocol)	VIE-VR-0233 (VLA1553 Final Product Air Shipping Validation Report)		
Finished Product, Packaging validation lots (b) (4) lots), Commercial Kit), Commercial shipping route (Road/Air for Europe and US, with EPR evaluation)	Ongoing	Ongoing	Ongoing	Report will be submitted by end August 2023 (Response to IR#42, 7a)
Shock/Drop Testing (Pallet from Finished Product, Packaging validation lot)	Ongoing	Ongoing	Ongoing	Report will be submitted by end August 2023 (Response to IR#42, 7b)

ERP – Essential Performance Requirements

CBER Response to Question #6:

CBER referred Valneva to IR #55 communicated on June 23, 2023, and reiterated its request that Valneva provide a response within the requested time frame.

9. Wrap-up and Action Items:

CBER summarized the following Action Items:

- CBER will provide contact information for CBER Lot Release; for Advertising, Promotional and Labeling branch and for NDC acceptability.
- Valneva acknowledged the requirement for a 2nd post marketing effectiveness study communicated in IR #50, and CBER will reach out with details for a telecon between CBER senior management and Valneva.
- Valneva will be providing a timely response to IR #55.

- A summary of the late cycle meeting will be provided within 30 days.

The meeting concluded at 3:38 PM EDT.

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.