



Memorandum

DATE August 23, 2023

FROM Triet M. Tran, PharmD, BCSCP, Consumer Safety Officer
Bioresearch Monitoring Branch (BMB)
Division of Inspections and Surveillance (DIS)
Office of Compliance and Biologics Quality (OCBQ)
Telephone: 240-425-3201

THROUGH Dennis T. Cato, Chief BMB

THROUGH Carrie M. Mampilly, MPH, Director DIS

TO Sudhakar Agnihothram, PhD, Chair, BLA STN 125777/0
Sixun Yang, MD, Clinical Reviewer
Konstantin Virnik, PhD, RPM
Georgeta Crivat, PhD, RPM

SUBJECT Bioresearch Monitoring Final Review Memo
SPONSOR Valneva Austria GmbH.
PRODUCT IXCHIQ (Chikungunya Vaccine, Live (VLA1553))
BLA STN 125777/0

Final Summary Statement

Bioresearch Monitoring (BIMO) inspections were issued for three domestic Clinical Investigator (CI) sites participating in the conduct of study Protocol VLA1553-301. The inspections did not reveal significant problems impacting the data submitted in support of this original Biologics License Application (BLA).

Background

BIMO inspection assignments were issued for three CI sites that participated in the conduct of study Protocol VLA1553-301. The sites were selected based on previous inspectional history, geographic location, and the data submitted in the BLA. The BLA review committee concurred with the sites selected for inspection. The inspection assignments were issued for the following study protocol:

Protocol VLA1553-301- *A multicenter, randomized, placebo-controlled, double-blinded pivotal study to evaluate safety and immunogenicity of a live-attenuated chikungunya virus vaccine candidate (VLA1553) in adults aged 18 years and above.*

BIMO CI inspections were conducted in accordance with FDA's Compliance Program (CP) 7348.811, Inspection Program for CI. The study was conducted at 43 study sites across the United States, enrolling a total of 4,128 subjects. The three CI study sites inspected in support of this BLA enrolled a total of 460 subjects, accounting for approximately 11% of all subjects enrolled in the study.

The inspection assignment included specific questions related to the study protocol, and the information submitted in the BLA was compared to source documents at each inspected site. The inspections verified the data reported in the BLA, including, but not limited to, subject eligibility, protocol deviations, study drug administration, primary efficacy endpoint, and adverse events for the subjects enrolled at the clinical sites.

Inspection Outcome

No significant objectionable inspectional findings were observed during the inspection. The table below summarizes the BIMO inspections:

Site ID	Number of subjects randomized	Location	483 Issued	Final Inspection Classification
06	67	Ernie Riffer, M.D. Synexus – Central Phoenix Medical Clinic 7600 North 15th Street Phoenix, Arizona 85020	Yes	Voluntary Action Indicated (VAI)
19	232	Maria Bermudez, M.D Suncoast Research Associates 9260 Sunset Drive Suite 107 Miami, Florida 33173	Yes	VAI
32	161	Beth E. Safirstein, M.D Velocity Clinical Research 911 E Hallandale Beach Blvd, Hallandale Beach, FL 33009	Yes	VAI

Noteworthy inspectional findings

The inspections did not reveal substantiative issues that impact the data submitted in the BLA.

Sponsor Issues

No significant sponsor issues were noted.

Clinical Investigator Issues

A Form FDA 483 (FDA 483), Inspectional Observation, was issued to Dr. Ernie Riffer, MD at site 06. The FDA investigator discovered instances where the dates of the body temperatures recorded in the eDiary were not accurately reported in the electronic Case Report Form (eCRF). Additionally, the investigator found that visit data was not recorded in the eCRF database within one business day after collection, and not all data recorded in

the eDiary was retained for the required two-year period after the marketing application is approved for the drug.

An FDA 483 was issued to Dr. Maria Bermudez, MD at site 19. The FDA investigator discovered that there was one instance where the wrong IP kit was administered to a subject, and the freezer used for the storage of the serum samples had experienced temperature excursions outside of the range specified in the Protocol and Pharmacy Manual.

An FDA 483 was issued to Beth E. Safirstein, MD at site 32. The FDA investigator discovered that the fridge and freezer used for the storage of the IP and serum samples had experienced temperature excursions outside of the range specified in the Protocol and Pharmacy Manual.

Appropriate corrective actions were implemented at each inspected site, to correct the deficiencies from the inspectional observations.

Financial Disclosure

The CI CP directs the FDA investigators to ask the CI if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouses and dependent children, and if and when the information was last updated. The information submitted to the BLA was verified at the inspected sites and no deviations were found in the submitted data.

Administrative follow-up

No administrative follow-up is warranted at this time. Should you have any questions about the contents of this memo or any aspect of BIMO, please contact me at 240-425-3201.

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