



U.S. FOOD & DRUG
ADMINISTRATION

DATE: May 8, 2024

FROM: Peter Lenahan, DC, PhD, MPH
Bioresearch Monitoring Branch (BMB)
Division of Inspections and Surveillance (DIS)
Office of Compliance and Biologics Quality (OCBQ)

THROUGH: Dennis Cato, Associate Director for Bioresearch Monitoring

THROUGH: Carrie Mampilly, MPH, Director, Division of Inspections and Surveillance (DIS)

TO: CBER Connect STN 125814/0, IND 19316
Tatiana Claro da Silva, PhD, Chair
Nicholas Geagan, MD, Clinical Reviewer
Diana Oram, PhD, RPM
Margaret Dayhoff-Brannigan, PhD, RPM
Hilda Grabczewski, PhD, RPM

SUBJECT: Bioresearch Monitoring Final Discipline Review Memo

SPONSOR: Merck, Sharp and Dohme, Inc.

PRODUCT: PNEUMOCOCCAL 21-VALENT CONJUGATE VACCINE (V116)

BLA/STN 125814/0

Final BIMO SUMMARY STATEMENT

Bioresearch Monitoring (BIMO) inspections were issued for two domestic and two foreign clinical investigators who participated in the conduct of Protocol V116-003. The inspections did not reveal substantive issues that impact the data submitted in this original Biologics License Application (BLA).

BACKGROUND

BIMO inspection assignments were issued for four clinical study sites that conducted the study protocol V116-003. The BLA clinical review committee concurred with the proposed sites. The sites were selected based upon sponsor-reported adverse events, subject deaths, protocol deviations, total numbers of enrolled subjects, previous BIMO inspection histories, BLA clinical review team recommendations, and clinical investigator financial disclosures.

The inspections were conducted in accordance with FDA's Compliance Program (CP) 7348.811, Inspection Program for Clinical Investigators. Information submitted in the BLA was compared to source documents at each inspected site. The inspection assignment also included specific questions concerning the clinical study.

PROTOCOL

Protocol Number: V116-003; Protocol Title: "A Phase 3, Randomized, Double-blind, Active Comparator-controlled Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of V116 in Pneumococcal Vaccine-naïve Adults".

BIMO INSPECTIONS SUMMARY

A Form FDA-483 was issued for site 0068 at close of the inspection and the inspection was classified Voluntary Action Indicated (VAI). All other inspections were classified No Action Indicated (NAI).

The below table summarizes site information and outcomes from the BIMO inspections:

Site Number	Location	Form FDA-483 Issued	Final Classification
1003	Diepenbeek, Belgium	No	NAI
3102	Rotorua, Bay of Plenty, New Zealand	No	NAI
0082	Lewisville, Texas	No	NAI
0068	Houston, Texas	Yes	VAI

SIGNIFICANT INSPECTIONAL FINDINGS

A Form FDA 483 was issued to Study Site 0068 at the conclusion of the inspection. Specifically, the investigator failed to supervise the investigation. The subject inclusion/exclusion eligibility for subjects [REDACTED] was assessed and signed by a nurse practitioner. The Inclusion/Exclusion Criteria section 8.1.2 of the protocol states "All inclusion and exclusion criteria will be reviewed by the investigator, who is a qualified physician, to ensure that the participant qualifies for the study". No significant data integrity issues were observed.

SPONSOR/MONITORING ISSUES

No significant sponsor monitoring issues were identified during the above inspections.

FINANCIAL DISCLOSURE

The Clinical Investigator Compliance Program directs the FDA investigator to ask the clinical investigator if, and when, they disclosed information about their financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children, as well as if and when the information was last updated. The information submitted to the BLA was verified for each of the inspected clinical study sites.

ADMINISTRATIVE FOLLOW-UP

Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me by telephone at (301) 837-7156 or by email at Peter.Lenahan@fda.hhs.gov.

Respectfully,

Peter Lenahan, DC, PhD, MPH
CDR, U.S. Public Health Service
Senior Regulatory Reviewer

DISTRIBUTION:

Electronic Copies:

CBER Connect: STN 125814/0
Tatiana Claro da Silva, PhD, Chair
Nicholas Geagan, MD, Clinical Reviewer
Sarah Benke, MD, Clinical Reviewer
Diana Oram, PhD, RPM
Margaret Dayhoff-Brannigan, PhD, RPM
Hilda Grabczewski, PhD, RPM
Carrie M. Mampilly, MS, DIS
Dennis T. Cato, Branch Chief, BMB
Char-Dell Edwards for the Chron File
cberbimonotification@fda.hhs.gov
ORA BIMOE Correspondence