



Memorandum

DATE: May 25, 2021

TO: Qun Wang, PhD, BLA Committee Chair
Anuja Rastogi, MD, Clinical Reviewer
Taruna Khurana, PhD, BLA RPM
Tatiana Claro, PhD, BLA RPM

FROM: Malcolm Nasirah, PharmD, MS, Regulatory Reviewer
Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH: Dennis T. Cato, Chief, Bioresearch Monitoring Branch

THROUGH: Carrie M. Mampilly, MPH., Director, Division of Inspections and Surveillance

SUBJECT: Bioresearch Monitoring Final Discipline Review Memo

PRODUCT: Pneumococcal 15-Valent Conjugate Vaccine [CRM197 Protein], (b) (4)
V114

SPONSOR: Merck Sharp & Dohme Corp.
BLA STN: 125741/0

REVIEW SUMMARY

Bioresearch Monitoring (BIMO) inspections were issued for three clinical study sites that participated in the conduct of study Protocol 019-00. The inspections did not reveal substantive issues that impact the data submitted in this Biologics License Application (BLA).

BACKGROUND

Three U.S. clinical study sites conducting the phase III study Protocol 019-00 were identified for BIMO inspections. The sites were selected based upon previous BIMO inspection history, sponsor-reported adverse events, protocol deviations, and total number of subjects enrolled.

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 019-00: *A Phase 3, Multicenter, Randomized, Double-blind, Active Comparator-controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of V114 in Healthy Adults 50 Years of Age or Older (PNEU-AGE)*

The sponsor reported a total of 1205 subjects enrolled under clinical study Protocol 019-00 at 30 centers in five countries, and of the 1205 enrolled subjects, 1190 completed the study. The inspected sites comprise about 14% of the total subjects enrolled under Protocol 019-00.

BIMO INSPECTIONS SUMMARY

No significant BIMO inspectional findings were noted. The below table summarizes site information and outcomes from the BIMO inspections.

Study Site #	Firm Name	Location	FDA Form 483 Issued	Inspectional Final Classification
1007	George Freeman, MD	Newport News, VA	No	NAI
1012	Purvi Mehra, MD	San Diego, CA	No	NAI
0117	Enrique Pelayo, MD	Miami, FL	No	NAI

NAI = No Action Indicated

INSPECTIONAL FINDINGS:

Site 1012:

- a. There is no documentation that the protocol required (b) (4) training was completed for study staff and/or study subjects. Per the site, the training was conducted “verbally.”
- b. Daily temperature(s) recorded in error by subject (b) (6) in the (b) (4) were submitted in the application data line listings.

SPONSOR/MONITORING ISSUES

No significant sponsor or 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 he/she disclosed information about his/her 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 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 at 301-796-6667 or Malcolm.Nasirah@fda.hhs.gov.

Malcolm Nasirah, PharmD, MS, BCGP
Consumer Safety Officer