Memorandum

DATE: March 18, 2020

TO: Joe Temenak, PhD, BLA Committee Chair
Anuja Rastogi, MD, Clinical Reviewer
Ramachandra Naik, PhD, BLA RPM
Mike Smith, PhD, BLA RPM
Nikunj Sharma, PhD, BLA RPM

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

THROUGH: Dennis Cato, Chief, Bioresearch Monitoring Branch

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

SUBJECT: Bioresearch Monitoring Discipline Review
BLA STN: 125701/0

PRODUCT: Meningococcal (Groups A, C, Y, W) Polysaccharide Tetanus Toxoid Conjugate Vaccine

SPONSOR: Sanofi Pasteur Inc.

REVIEW SUMMARY

Bioresearch Monitoring (BIMO) inspections were issued for four U.S. clinical study sites that participated in the conduct of Protocols MET 35, MET 43, and MET 49. The inspections did not reveal any issues that impact the data submitted in this original Biologics License Application (BLA).

BACKGROUND

Four U.S. clinical study sites under phase 3 Protocols MET 35, MET 43, and MET 49 were identified for BIMO inspections. The BLA review committee concurred with the proposed sites. Sites were selected based upon inspection history, numbers of subjects enrolled, and types of studies conducted at each site.

The inspections were conducted in accordance with FDA's Compliance Program Guidance Manual (CPGM) 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 conduct of the clinical study.

Protocol(s) inspected:

Protocol MET 35
Phase III, modified double-blind, randomized, parallel-group, active-controlled, multi-center trial to evaluate the immunogenicity and describe the safety of MenACYW conjugate vaccine compared to a licensed quadrivalent meningococcal conjugate vaccine in healthy children 2 to 9 years of age in the United States and Puerto Rico (MET 35).

Protocol MET 43
Phase III, modified double-blind, randomized, parallel-group, active-controlled, multi-center study to evaluate immune lot consistency of MenACYW conjugate vaccine, evaluate the immune non-inferiority versus Manactra®, and describe the safety and additional immunogenicity of these study vaccines in adolescents and adults aged 10 to 55 years in the United States (MET 43).

Protocol MET 49
Phase III, Modified double-blind, randomized, parallel-group, active-controlled, multi-center trial to compare the immunogenicity and safety of MenACYW conjugate vaccine to Menomune®- A/C/Y/W- 135 in adults ≥ 56 years of age in the United States (MET 49).

The sponsor reported a total of 5,244 subjects were enrolled collectively under clinical study Protocols MET 35, MET 43, and MET 49. The inspected sites comprised of approximately 5.6% of the total subjects dosed with the study drug under Protocols MET 35, MET 43, and MET 49.

INSPECTED SITES

Study Site#	Site Name	Location	Form FDA 483 Issued?	Inspection Final Classification
81	Coastal Carolina Research Center	Mt. Pleasant, SC	No	NAI*
69	Emmaus Research Center	Anaheim, CA	No	NAI
56	Heartland Research Associates	Wichita, KS	No	NAI
27	The Children's Clinic of Jonesboro	Jonesboro, AR	No	NAI
26	Emmaus Research Center	Anaheim, CA	No	NAI
22	Coastal Carolina Research Center	Mt. Pleasant, SC	No	NAI

* NAI - No Action Indicated

INSPECTIONAL FINDINGS
The results from the inspections showed no significant issues.

SPONSOR/MONITORING ISSUES

BIMO submitted IRs on May 22nd 2020 and May 29th 2020. The Sponsor responded by submitting Amendments 2 and Amendments 3 to the submission. BIMO reviewed these Amendments and found that the Sponsor's response to the Information Requests was adequate. There are no outstanding issues.

FINANCIAL DISCLOSURE

The Clinical Investigator Compliance Program (CPGM 7348.811) 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 investigators.

ADMINISTRATIVE FOLLOW-UP

No administrative follow-up is pending for this review. 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

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