

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

DATE August 31, 2015

FROM Anthony Hawkins, Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Chief, Bioresearch Monitoring Branch

THROUGH Gilliam Conley, Director, Division of Inspections and Surveillance

TO Brenda Baldwin, BLA Committee Chair
Sarah Browne, Clinical Reviewer
Kirk Prutzman, RPM
Ted Garnett, RPM

SUBJECT Bioresearch Monitoring Final Discipline Review
BLA: STN 125510-0
IND: 14368
PRODUCT: Influenza Vaccine, Adjuvanted
SPONSOR: Novartis Vaccines and Diagnostics, Inc.

REVIEW SUMMARY

Bioresearch Monitoring inspections of one foreign and two U.S. clinical investigator study sites were conducted in support of this Biologics Licensing Application (BLA). The inspections did not reveal substantive problems that impact the data submitted in this BLA.

BACKGROUND

One foreign and two U.S. clinical investigator study sites under phase III clinical study protocol V70_27 were identified for Bioresearch Monitoring inspections. The BLA review committee concurred with the proposed sites. The sites were selected based upon numbers of enrolled study subjects, prior FDA inspection history and numbers and types of adverse events and protocol deviations.

Protocol inspected: *A Phase III, Randomized, Controlled, Observer-Blind, Multicenter Study to Evaluate the Safety and Immunogenicity and the Consistency of Three Consecutive Lots of a MF59C.1 Adjuvanted Trivalent Subunit Influenza Vaccine in Elderly Subjects Aged 65 Years and Older* (Protocol V70_27)

Clinical study protocol V70_27 was conducted at 21 U.S. and 17 foreign clinical sites where a total of 7109 subjects were enrolled, with 7082 subjects randomized and vaccinated. The three inspected sites comprise approximately 11% of the total subjects enrolled under the protocol.

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 included specific questions concerning the clinical study.

INSPECTIONS

Bioresearch Monitoring inspections were conducted at the following clinical study sites:

Study Site #	Site Name	Location	Form FDA 483 Issued?	Final Inspection Classification
326	PMG Research of Raleigh, LLC	Raleigh, NC	No	NAI
332	PMG Research of Winston-Salem	Winston-Salem, NC	No	NAI
206	Centro de Atencion e Investigacion Medica (CAIMED)	Bogota, Colombia	No	NAI

NAI = No Action Indicated

INSPECTION FINDINGS

The results from the inspections showed only a few minor problems.

Study Records:

The **Site 206** inspection showed discrepancies involving documentation of verbal adverse event reports for six subjects reviewed during the inspection, along with missing study delegations for various individuals who performed study tasks. The **Site 326** inspection revealed transcription discrepancies between source documents and electronic case report form entries involving adverse events for two study subjects.

SPONSOR ISSUES

No sponsor or monitoring issues were noted.

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 investigators.

ADMINISTRATIVE FOLLOW-UP:

We issued information letters to each of the above clinical investigators. Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at 240-402-8950.

Anthony Hawkins
Consumer Safety Officer

Distribution

Electronic Copies:

Upload to Application Folder in EDR
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