

MEMORANDUM

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

DATE: April 12, 2016

FROM: Haecin Chun
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: Pei Zhang, BLA Committee Chair
Charles Maplethorpe, BLA Clinical Reviewer
Yu Do, RPM

SUBJECT: Bioresearch Monitoring Final Discipline Review
SPONSOR: ADMA Biologics, Inc.
PRODUCT: Immune Globulin Intravenous, Human, 10% Liquid
BLA: 125590/0

FINAL SUMMARY STATEMENT

Bioresearch Monitoring (BIMO) inspections of three clinical investigators in support of this Biologics Licensing Application (BLA) did not reveal substantive problems that impact the data submitted in the application.

BACKGROUND

Three clinical investigator inspection assignments were issued in support of this Biologics License Application (BLA). The protocol identified for the BIMO inspections was *An Open Label, Multicenter Study to Evaluate the Pharmacokinetics, Efficacy, and Safety of RI-002 (IGIV) in Subjects with Primary Immunodeficiency Diseases (Protocol: ADMA-003)*.

Protocol ADMA-003 was conducted at a total of ten study sites in the United States. A total of 59 subjects were enrolled and 40 of these subjects were in the 4-week infusion cycle group and 19 subjects in the 3-week infusion cycle group. The three clinical study sites selected for BIMO inspection represented 54% (32) of the subjects enrolled. The clinical sites were selected based on subject enrollment, previous inspectional history and geographic location, as well protocol deviations and adverse events.

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 of the inspected study sites. The inspection assignment included specific questions concerning the clinical study.

INSPECTIONS

The following table summarizes the results of the BIMO inspections for the clinical study sites selected in support of this BLA:

SITE NUMBER	SITE LOCATION	FORM FDA 483	FINAL CLASSIFICATION*
103	Midlands Pediatrics Papillion, NE	Issued	VAI
104	The South Bend Clinic South Bend, IN	Issued	VAI
111	IMMUNOe Health Center Centennial, CO	Not Issued	NAI

*NAI = No Action Indicated; VAI = Voluntary Action Indicated

SIGNIFICANT INSPECTIONAL FINDINGS

No significant inspectional findings were noted; however, the following items were noted:

- The **Site 103** did not report several adverse events to the sponsor and did not obtain prior approval from the ADME Medical Director for one subject taking a prohibited medication following the last infusion of RI-002 (Infusion Cycle #13), as required by the protocol; and
- The **Site 104** clinical investigator did not review the adverse event reports and lab data promptly. Some reviews were performed on the day before the inspection.

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, and 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.

Please contact me at (240) 402-8038 if you have any questions about this memo or any aspect of Bioresearch Monitoring.

Haecin Chun
Consumer Safety Officer

DISTRIBUTION

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