

BIMO Final Summary Memo, July 19, 2011 - Bivigam

MEMORANDUM
SERVICES

DEPARTMENT OF HEALTH AND HUMAN

Public Health Service

Food and Drug Administration

Center for Biologics Evaluation and Research

DATE July 19, 2011

FROM Lillian Ortega, Bioresearch Monitoring, HFM-664
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Bioresearch Monitoring Branch Chief, HFM-664

TO Michael Kennedy, HFM- 345, Chair person, BLA Committee
Mitchell Frost, HFM-392, Clinical Reviewer, BLA Committee
Pratibha Rana, HFM-380, RPM, BLA Committee

SUBJECT Bioresearch Monitoring Inspection Results

Sponsor: Biotest Pharmaceuticals Corporation

BLA/STN: 125389/0

Product: Immune Globulin Intravenous (Human) 10% (Nabi- IGIV)

SUMMARY STATEMENT

The results of Bioresearch Monitoring inspections of four clinical sites did not reveal problems that impact the data submitted in the application.

BACKGROUND

There were four (4) clinical investigator inspections performed in support of the Biologics License Application (BLA) supplement and were conducted in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators. The inspections represented approximately 39% of the total subjects enrolled in **NABI-7101**. The inspection assignment included specific questions in reference to the study protocol and verification of the study data on safety and efficacy endpoints submitted by the sponsor in the BLA supplement.

Site 009: The sponsor reported the termination of Site 009 on May 20, 2008 as a result of findings from two interim site monitoring visit. The monitoring visits identified protocol deviations and violations including the failure to adhere to the study protocol, enrollment of subjects that met study exclusionary criteria and failure to report a serious adverse event per Good Clinical Practice guidelines. Due to the deviations and violations mentioned above, the sponsor made the decision to exclude Site 009 from the Intent to Treat (ITT) population but allow the subjects to be included in the safety assessment of the Biologics Licensing Application.

Site #	Study Site	Location	Subjects Enrolled	Form FDA 483 Issued	Inspection Final Classification
007	Children's Hospital Los Angeles	Los Angeles, California	7	Yes	VAI

Site #	Study Site	Location	Subjects Enrolled	Form FDA 483 Issued	Inspection Final Classification
009	Montefiore Medical Center	Bronx, New York	5	No	NAI
014	Bellingham Asthma, Allergy & Immunology Clinic	Bellingham, Washington	5	Yes	VAI
019	Allergy & Asthma Center	Toledo, Ohio	8	No	NAI

NAI- No Action Indicated ; VAI – Voluntary Action Indicated

PROTOCOL: NABI-7101

STUDY TITLE: Open Label, Phase III Safety, Efficacy and Pharmacokinetic Study of NABI-IGIV 10% [Immune Globulin Intravenous (Human)] in subjects with Primary Immune Deficiency Disorders (PIDD) February 17, 2009

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 subinvestigators, spouse(s) and dependent children, and if and when the information was updated. The inspections were conducted in accordance with the compliance program.

SPONSOR/MONITOR ISSUES

No sponsor or monitoring issues noted at the sites.

NOTEWORTHY INSPECTIONAL FINDINGS

1. Failure to ensure that the investigation was conducted according to the investigational plan.

- Protocol Inclusion Criteria states the subject must currently be on an IGIV replacement therapy at a fixed interval and dosage between 300 and 800 mg/kg. Site 014 enrolled subject # --(b)(6)--- who did not meet eligibility dosing requirements at screening. The same subject received a total IGIV infusion of 275 mg/kg throughout the study. The study protocol states each subject will receive a total IGIV infusion of 300 – 800 mg/kg per month.
- The Protocol states the initial infusion rate will be 30mL/kg/hr (30mg/kg/hr) for 10 minutes and if well tolerated, the rate can be increased to 0.5 mL/kg/hr (50 mg/kg/hr) for 20 minutes. Site 014 increased infusion rates prior to the 10 minutes (initial rate) or 20 minutes (subsequent rate increases) for 3 of the 5 subjects enrolled at the site.
- The Protocol states all subjects are required to give their informed consent prior to the performance of any clinical activities or procedures. The informed consent form for Site 007 had 3 versions during the study, and 5 of the 7 subjects enrolled in the study did not sign the most current Institutional Review Board (IRB) approved consent forms at their next visits for conducted study drug infusions and/ or study related testing.

Site 009: The inspection revealed that the clinical investigator conducted the protocol required safety follow up or documented the site's attempts to do so. Due to the discontinuation of the study some subjects were unwilling to return to the site.

For the four clinical sites inspected, there was no evidence of under reporting of adverse events and no discrepancies noted between the source documents, CRF's and the data submitted in the BLA.

BIMO ADMINISTRATIVE FOLLOW-UP

Informational letters will be issued to the clinical investigators. Please contact me at 301-827-6335 if you have any questions about this memorandum or any aspects of Bioresearch Monitoring.

Lillian Ortega

Consumer Safety Officer

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