

MEMORANDUM

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

DATE January 5, 2016

FROM Erin McDowell, Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Chief, Bioresearch Monitoring Branch

Gilliam Conley, Director, Division of Inspections and Surveillance

TO Michael Kennedy, BLA Committee Chair
Laurence Landow and Clinical Reviewer
Christopher Hooban, and Nannette Cagungun, RPM

SUBJECT Bioresearch Monitoring Summary Review Memo
BLA: STN 125587/0
IND: 14001 and 14121

PRODUCT Panzyga (NewGam)
SPONSOR: Octapharma AG

REVIEW SUMMARY

Bioresearch Monitoring (BIMO) inspections of two foreign and three domestic clinical investigators were conducted in support of this supplement Biologics Licensing Application (BLA). The bioresearch monitoring inspections did not reveal substantive problems that impact the data submitted in the Biologics Licensing Application (BLA).

BACKGROUND

The BIMO member of the review committee proposed two foreign and three domestic clinical sites to be inspected for this application. The selections were based on number of subjects enrolled, previous inspection history, and geographic location. The review committee concurred with the proposed sites. The five sites selected for Bioresearch Monitoring (BIMO) inspection, represented ~39% of the subjects enrolled in NGAM-01 (52% NGAM-05) and 17% of the subjects enrolled in NGAM-02. 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 clinical site. The inspection assignment included specific questions concerning the clinical studies NGAM-01 and NGAM-05 or NGAM-02.

STUDIES:

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Protocol NGAM-01: Clinical Study To Evaluate The Efficacy, Pharmacokinetics And Safety Of Immunoglobulin Intravenous (Human) 10% (Newgam) In Patients With Primary Immunodeficiency Diseases (NCT#01012323; January 2010 to June 2012)

Protocol NGAM-05: Clinical Study To Evaluate The Safety And Tolerability Of Immunoglobulin Intravenous (Human) 10% (Newgam) Administered At High Infusion Rates To Patients With Primary Immunodeficiency Diseases (NCT#01313507; May 2011 to September 2012)

Protocol NGAM-02: Prospective, open-label, non-controlled, multicentre, phase III clinical study to evaluate the efficacy and safety of immunoglobulin intravenous (human) 10% (NewGam) in primary immune thrombocytopenia (NCT#01349790; October 2011 to July 2013)

INSPECTIONAL FINDINGS

The following table summarizes BIMO inspections that were conducted:

Site#	Study Site	#Subjects	Location	Form FDA 483 Issued	Final Classification
Studies NGAM-01 (and NGAM-05)					
01	Rush University	9 (4)	Chicago, Illinois	Yes	Voluntary Action Indicated
02	Cardinal Glennon Medical Center	6 (2)	St. Louis, Missouri	Yes	Voluntary Action Indicated
14	Seattle Children's Hospital	5 (5)	Seattle, Washington	Yes	Voluntary Action Indicated
Study NGAM-02					
01	Charite University	3	Berlin Germany	Yes	Voluntary Action Indicated
08	University Hospital Brno	4	Czech Republic	No	No Action Indicated

The inspection of NGAM-01 and NGAM-05 Site#01 revealed that over the course of the study there were multiple instances when temperature excursions for the investigative product storage occurred without being detected for prolonged periods of time. There were several corrective actions implemented. The investigational product record shows amount quarantined when temperature excursion was uncovered but does not note if any of the product was used during the time the temperature was out of range.

The inspection of studies NGAM-01 and NGAM-05 at Site#2 revealed the following: for at least 2 subjects, the study drug dose was not increased when the subject's body weight increased by 5%; concomitant medications were not documented appropriately for 2 subjects; and an outdated informed consent form was used for 1 subject. Several items were discussed with the clinical investigator at the close of the inspection, including good documentation practices, medication lists being accurate, and appropriate adverse event reporting.

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The inspection of studies NGAM-01 and NGAM-05 Site #14 revealed once instance of forbidden therapy (vaccination) for two subjects, one instance of an incomplete subject name on the informed consent form, and two subjects who received infusion out of window prior to a pharmacokinetic visit.

The inspection of study NGAM-02 Sites# 01 revealed that one subject was not eligible for enrollment on study and a dose was miscalculated for another subject.

The inspection for study NGAM-02 Site # 08 did not reveal any deviations to the regulations.

Sponsor Monitoring Issues

No issues were identified.

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 sites.

ADMINISTRATIVE FOLLOW-UP:

Information letters were issued to the five clinical investigator sites. Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at (240) 402-9140.

Erin McDowell
Consumer Safety Officer

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