

MEMORANDUM

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

DATE January 6, 2017

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

THROUGH Patricia Holobaugh, Chief, Bioresearch Monitoring Branch

Carrie Mampilly, Director, Division of Inspections and Surveillance

TO Chava Kimchi-Sarfaty, Ph.D., BLA Committee Chair
Megha Kaushal, M.D., BLA Clinical Reviewer
Edward Thompson, BLA RPM

SUBJECT Bioresearch Monitoring Final Discipline Review
BLA: STN 125611-0
Product: Coagulation Factor IX (Recombinant), GlycoPEGylated
Sponsor: Novo Nordisk, Inc.

REVIEW SUMMARY

Bioresearch monitoring inspections of four clinical investigator study sites were conducted in support of this Biologics Licensing Application (BLA). Results from the inspections did not reveal substantive problems that impact the data submitted in the BLA.

BACKGROUND

Four clinical investigator study sites under phase 3 study protocol NN7999-3747 were identified for Bioresearch Monitoring inspections. The BLA review committee concurred with the proposed sites. Sites were selected based upon numbers of enrolled study subjects and prior FDA inspection history.

Protocol inspected:

A multi-centre, single-blind trial evaluating safety and efficacy, including pharmacokinetics, of NNC-0156-0000-0009 when used for treatment and prophylaxis of bleeding episodes in patients with haemophilia B (Protocol NN7999-3747)

The sponsor reported that 40 clinical sites screened subjects under protocol NN7999-3747 and of those, 39 enrolled individuals for participation in the study. The study was conducted at 39 clinical sites in 13 countries. A total of 86 subjects were screened and of those, 74 enrolled and received study treatment. Sixty seven subjects completed the study. The inspected sites comprise approximately 12% 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
104	Mount Sinai Hospital	New York, NY	No	NAI
106	Children's Hospitals and Clinics of Minnesota	Minneapolis, MN	No	NAI
114	St. Michael's Medical Center	Newark, NJ	No	NAI
116	Gulf States Hemophilia & Thrombophilia Center	Houston, TX	No	NAI

NAI = No Action Indicated

INSPECTION FINDINGS

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

Protocol compliance:

The site 106 clinical investigator did not report several adverse events for one subject including cough, sneezing and runny nose.

Study Records:

The site 116 study records showed conflicting entries for one subject who did not consent to factor IX (FIX) genetic testing. The sponsor reported this protocol deviation to FDA, as part of the BLA submission.

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 a letter 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