



Memorandum

DATE: October 15, 2018

TO: Andrey Sarafanov, Ph.D., BLA Committee Chair
Najat Bouchkouj, M.D., BLA Committee Clinical Reviewer
Jean Dehdashti, MSc, BLA RPM

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

THROUGH: Dennis Cato, Chief, Bioresearch Monitoring Branch

THROUGH: Carrie Mampilly, M.P.H., Director, Division of Inspections and Surveillance

SUBJECT: Bioresearch Monitoring Discipline Review
BLA STN: 125671/0
PRODUCT: Antihemophilic Factor (Recombinant), GlycoPEGylated
SPONSOR: Novo Nordisk, Inc.

REVIEW SUMMARY

Bioresearch Monitoring (BIMO) inspections were issued for three foreign and two domestic clinical study sites that participated in the conduct of Protocol NN7088-3859. The inspections did not reveal any issues that impact the data submitted in this original Biologics License Application (BLA).

BACKGROUND

Three foreign and two domestic clinical study sites under phase 3 Protocol NN7088-3859 were identified for BIMO inspections. Foreign study sites did not conduct the protocol under the corresponding Investigational New Drug (IND) Application (IND 14410). The BLA review committee concurred with the proposed sites. The sites were selected based upon numbers of enrolled study subjects and prior FDA inspection history.

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 also included specific questions concerning the clinical study.

Protocol inspected:

Protocol: *A Multi-national Trial Evaluating Safety and Efficacy, including Pharmacokinetics, of NNC 0129-0000-1003 when Administered for Treatment and Prophylaxis of Bleeding in Patients with Haemophilia A (pathfinder™ 2) – Protocol NN7088-3859*

The sponsor reported a total of 215 subjects were screened under clinical study Protocol NN7088-3859 at 77 study sites in 22 countries. Of those, 186 subjects were dosed with the study drug, of which 25 were adolescents aged 12 – 17 years. The inspected sites comprise approximately 12% of the total subjects dosed with the study drug under Protocol NN7088-3859.

INSPECTED SITES

Study Site#	Site Name	Location	Form 483 Issued?	Inspection Final Classification
852	KD Haemophilia Centre & Thrombosis Unit	London, Great Britain	No	NAI
854	Oxford Haemophilia Centre	Oxford, Great Britain	No	NAI
856	Hemophilia Centre	Basingstoke, Great Britain	No	NAI
909	Children's Hospitals and Clinics of Minnesota	Minneapolis, Minnesota	No	NAI
914	Vanderbilt Clinical Trials Center	Nashville, Tennessee	No	NAI

INSPECTIONAL FINDINGS

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

SPONSOR/MONITORING ISSUES

The protocol NN7088-3859 consent documents reviewed during three of the above inspections at sites 852, 854, and 856 did not include a statement that notes the possibility that FDA may inspect the study records, as required.

FINANCIAL DISCLOSURE

The Clinical Investigator Compliance Program (CPGM 7348.811) 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

DISTRIBUTION

Scanned/Electronic Copies:

Upload to Application Folder in EDR

Andrey Sarafanov

Najat Bouchkouj

Jean Dehdashti

Carrie Mampilly

Dennis Cato

Colonious King

cberbimonotification@fda.hhs.gov

ORAHQ BIMO Inspection POC

Craig Rybus, FDA Investigator

Ruth Williams, FDA Investigator

Ladislav Kermet, FDA Investigator

Sharon Matson, FDA Investigator

LauraLee Staples, FDA Investigator

Draft: Hawkins: 10/15/2018

Reviewed: Cato: 10/23/2018
