

MEMORANDUM

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

DATE: January 05, 2016

FROM: Haecin Chun
Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH: Patricia Holobaugh, Bioresearch Monitoring Branch Chief

THROUGH: Gilliam Conley, Director, Division of Inspections and Surveillance

TO: Alexey Khrenov, Chair
Victor Baum, Clinical Reviewer
Thomas Maruna, RPM

SUBJECT: Bioresearch Monitoring Final Discipline Review Memo
SPONSOR: CSL Behring
PRODUCT: Antihemophilic Factor (Recombinant), Single Chain
BLA: 125591/0

FINAL SUMMARY STATEMENT

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

BACKGROUND

Three clinical investigator assignments were issued in support of this Biologics License Application (BLA). The protocol identified for review during the BIMO inspections was *A Phase I/III Open-label, Multicenter, Crossover Safety, Efficacy and Pharmacokinetic Study of Recombinant Coagulation Factor VIII (rFVIII) Compared to Recombinant Human Antihemophilic Factor VIII (rFVIII: INN: octocog alfa) in Subjects with Hemophilia A and a Repeat PK, Safety and Efficacy Study (CSL627_1001)*.

Protocol CSL627_1001 was conducted at a total of 54 study sites: nine sites in the United States and 45 sites outside of the United States. A total of 175 subjects were enrolled and 174 of these subjects were treated with rFVIII-SingleChain. Thirteen subjects participated in the surgical substudy. The three clinical study sites selected for inspection represented 19% (33) of the subjects enrolled. The clinical sites were selected based on subject enrollment, previous

inspectional history and geographic location.

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 this site. The inspection assignment included specific questions concerning the clinical study.

STUDY TITLE

A Phase I/III Open-label, Multicenter, Crossover Safety, Efficacy and Pharmacokinetic Study of Recombinant Coagulation Factor VIII (rFVIII) Compared to Recombinant Human Antihemophilic Factor VIII (rFVIII: INN: octocog alfa) in Subjects with Hemophilia A and a Repeat PK, Safety and Efficacy Study (**CSL627_1001**)

INSPECTION SITES

The following table summarizes the international clinical study sites where Bioresearch Monitoring inspections were conducted:

SITE LOCATION	SITE NUMBER	FORM FDA 483	FINAL CLASSIFICATION*
Charlotte Maxeke Johannesburg Academic Hospital Johannesburg, South Africa	7100001	Not Issued	NAI
Klinika Hematologii Nowotworow Krwi i Transplantacji Szpiku Wroclaw, Poland	6160014	Issued	VAI
Perpetual Succour Hospital Cebu, Philippines	6080001	Not Issued	NAI

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

SIGNIFICANT INSPECTIONAL FINDINGS

No significant inspectional findings were noted.

SPONSOR ISSUES

An Information Request (IR) letter was issued to CSL Behring on November 05, 2015, to obtain explanations regarding HIV-related data. The sponsor submitted a written response to the IR letter in an amendment on November 11, 2015. The response was discussed with the clinical reviewer and it was concluded that the sponsor adequately addressed the questions related to the HIV data.

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 clinical investigators at all sites in support of the BLA submission.

Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at 240-402-8038.

Haecin Chun
Consumer Safety Officer

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Draft: Chun, December 31, 2015

Reviewed: Drabick, January 04, 2016

Reviewed: Holobaugh, January 05, 2016

Reviewed Conley, January 05, 2016