Memorandum

DATE September 15, 2017

FROM Colonious King, Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality
Telephone: 240-402-8759 Fax: 301-595-1304

THROUGH Dennis Cato, Chief, Bioresearch Monitoring Branch

THROUGH Carrie Mampilly, Director, Division of Inspections and Surveillance

TO		
	Mikhail Ovanesov	Chair, Review Committee
	Poornima Sharma	Clinical Reviewer
	Mark Levi	RPM
	Edward Thompson	RPM

SUBJECT Bioresearch Monitoring Discipline Review Memo
BLA/STN: 125641/0
IND: 15183
Sponsor: LFB USA, Inc.
Product: Coagulation Factor VIIa (Recombinant), LR 769

FINAL SUMMARY STATEMENT:

Bioresearch Monitoring (BIMO) inspections were completed at one foreign and two domestic clinical study sites conducting study RB-FVIIa-006-13 in support of BLA 125641/0. The inspections did not reveal problems that impact the data submitted in this Biologics Licensing Application (BLA).

BACKGROUND

Three clinical investigators were inspected in support of the BLA and the inspections were conducted in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators. The inspection assignments were issued for protocol RB-FVIIa-006-13. The conduct of the protocol was reviewed during the BIMO inspections. The three clinical sites were selected based on subject enrollment, previous inspectional history, and geographic location.

The inspection assignment included specific questions related to the study protocol and verification of the study data on safety and efficacy endpoints submitted by the sponsor in the BLA. Study Protocol RB-FVIIa-006-13 was conducted at 13 study sites in nine countries. 29 subjects were screened for the study and 27 subjects were randomized in the study. The three

inspected sites randomized seven subjects, which is 26% of the total subjects randomized for the study. The information submitted in the BLA was compared to source documents at the inspection sites.

PROTOCOL REVIEWED

A Phase III study on the safety, pharmacokinetics and efficacy of coagulation factor VIIa (recombinant) in congenital hemophilia A or B patients with inhibitors to factor VIII or IX. (RB-FVIIa-006-13)

The table below summarizes the inspection results:

Site Numbers	Study Site	Location	Enrolled Subjects	Form FDA 483 Issued	Classification
9	Kyiv City Clinical Hospital #9	Kyiv city, Ukraine	5	No	NAI
19	Rush University	Chicago, Illinois	1	No	NAI
20	University of Colorado	Aurora, Colorado	1	No	NAI

NAI = No Action Indicated

FINANCIAL DISCLOSURE

The Clinical Investigator Compliance Program directs the FDA investigator to ask the clinical investigator if and when s/he disclosed information about her/his financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children including if and when the information was updated. The inspected study sites had a copy of the financial disclosure forms on hand for the clinical investigator and sub-investigators.

INSPECTIONAL FINDINGS

Sponsor/Monitor Issues

There were no sponsor/monitor issues identified at the study sites audited.

Clinical Investigator (CI) Study Site Issues

Study Site 9, 19, 20: A Form FDA 483 was not issued at close of the inspections and the inspections were classified as NAI. A review was conducted of testing records, regulatory binders, study specific standard operating procedures, and general study conduct. In addition, source documents were reviewed and the information was compared to the data tables submitted by the sponsor in the application. No discrepancy was found between source documents at the site and the data submitted by the sponsor in the application.

BIMO ADMINISTRATIVE FOLLOW-UP

Information letters were issued for the study sites inspected.

Please contact me should you have any questions about this memo or any aspect of Bioresearch Monitoring.

Colonious King
Consumer Safety Officer

Distribution

Electronic Copy

EDR	STN 125641/0
Mikhail Ovanesov	Chair, Review Committee
Poornima Sharma	Clinical Reviewer
Mark Levi	RPM
Edward Thompson	RPM
Carrie Mampilly	
Dennis Cato	
ORAHQ BIMO Inspection POC	
Laura Garcia	FDA Investigator
Linda Cherry	FDA Investigator
Lequita M. Mayhew	FDA Investigator

Draft: King: September 7, 2017
Reviewed: Drabick: September 8, 2017