

# Bioresearch Monitoring Discipline Review Memo, July 30, 2013 - ALPROLIX

## **MEMORANDUM**

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

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DATE July 30, 2013

FROM Anthony Hawkins, Bioresearch Monitoring, HFM-664

Division of Inspections and Surveillance

Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Bioresearch Monitoring Branch Chief, HFM-664

Gilliam Conley, Director, Division of Inspections and Surveillance, HFM-650

TO Nancy Kirschbaum, BLA Committee Chair, HFM-392

Stephanie Omokaro, Clinical Reviewer, HFM-392

Nisha Jain, Clinical Reviewer, HFM-392

Edward Thompson, RPM, HFM-380

SUBJECT Final BIMO Discipline Review Memo

BLA: STN 125444-0

IND: 13487

Product: Coagulation Factor IX (Recombinant), Fc Fusion Protein (rFIXFc)

Sponsor: Biogen Idec, Inc.

### **SUMMARY STATEMENT:**

Bioresearch monitoring inspections of five clinical study sites did not reveal significant problems that impact the data submitted in this biologics licensing application (BLA).

### **BACKGROUND**

The Bioresearch Monitoring Branch issued inspection assignments on February 28, 2013 covering five Protocol 998HB102 clinical investigators and study sites.

### **Inspections of Clinical Sites and Outcome:**

Location / Study site #	Enrolled subjects	Form FDA 483 issued?	Final inspection classification
Sacramento, CA / #102	10	No	NAI
Phoenix, AZ / #110	2	No	NAI
Chicago, IL / #150	6	Yes	VAI
Pittsburgh, PA / #300	6	No	NAI

Location / Study site #	Enrolled subjects	Form FDA 483 issued?	Final inspection classification
Seattle, WA / # 700	4	Yes	VAI

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

**STUDY TITLE:**

*B-LONG: An Open-label, Multi-center Evaluation of the Safety, Pharmacokinetics, and Efficacy of Recombinant, Long-acting Coagulation Factor IX Fc Fusion Protein (rFIXFc) in the Prevention and Treatment of Bleeding in Previously Treated Subjects with Severe Hemophilia B(Protocol 998HB102)*

**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 including if and when the information was updated. Each inspected study site had a copy of the financial disclosure forms on hand for clinical investigators and sub-investigators.

**SPONSOR ISSUES**

No sponsor or monitoring issues were noted.

**INSPECTIONAL FINDINGS**

The FDA investigators noted a few minor problems during the inspections.

**Study Records:**

The Master Drug Accountability and Subject Drug Accountability logs involving two separate product lots showed discrepant information, including greater numbers of study drug vials returned by one subject than those issued to the same individual. Four subjects had missing study documentation including adverse events, concomitant medications and eDiary training/review as discussed during their study visits. (Site 700) The clinical investigator did not sign the Agreement of Study Protocol version 2.0 document. The informed consent document reviewed during the inspection did not contain a statement that notes the possibility that FDA may inspect the study records, as required. (Site 150)

The study records showed numerous late data entries involving two subjects who used the protocol-specified electronic diary. The clinical investigator acknowledged difficulties with collecting all used and unused study drug vials from subjects as required. The inspection confirmed the Sponsor's previous report concerning the clinical investigator terminating a research nurse after discovering the nurse falsified study drug accountability documents involving 2 of the 6 total subjects enrolled at the site under Protocol 998HB102. The clinical investigator reported her findings to the IRB, prior to the FDA inspection. (Site 300)

The clinical investigator did not maintain study records pertaining to confidential subject responses to Quality of Life questionnaire #5. (Site 110) A one day BIMO inspection delay occurred because the clinical investigator did not maintain copies of each

subject's electronic case report form at the study site, as required by FDA regulations. (Site 102)

**Study Protocol Adherence, Clinical Investigator Responsibilities:**

The site had no documentation showing the study inclusion criteria applied to two enrolled subjects, one of whom participated in the study beyond the protocol-specified maximum of 52 weeks +/- 1 week. Two subjects had a total of at least six late study visits including late PK sampling on several occasions. (Site 700)

The clinical investigator did not report one subject's corticosteroid and lidocaine patch use as a protocol deviation and concomitant medication, respectively, as required. (Site 110)

**BIMO FOLLOW-UP**

We issued information letters to the inspected clinical investigators. Please contact me at (301) 827-6338 if you have any questions about this memo or any aspect of bioresearch monitoring.

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Anthony Hawkins  
Consumer Safety Officer

Distribution  
Application Number: 125444-0