

## Midcycle Meeting Summary

**Applicant:** OCTAPHARMA  
**STN:** 125555/0  
**Product:** Antihemophilic Factor (Recombinant) - rAHF  
 B-domain deleted recombinant Factor VIII (BDD-rFVIII)  
**Date:** 12:30 - 13:30 pm, November 18, 2014,  
**Chair:** Andrey Sarafanov, PhD  
**RPM:** Jiahua Qian, PhD

### CBER Participants:

#### Y; Attended meeting

	Reviewer	Att.	Branch Chief	Att.
RPM	Jiahua Qian	Y		
Chair/CMC	Andrey Sarafanov	Y	Tim Lee	Y
CMC	Nancy Kirschbaum	Y		
CMC	Misha Ovanesov			
CMC	Yideng Liang	y		
CMC	Ze Peng	y		
Clinical	Lisa Faulcon(on leave)		Nisha Jian	
APLB	Loan Nguyen	Y	Lisa Stockbridge	
Stat	Min Lin	Y	Renee Rees Boguang Zhen	Y Y
BIMO	Colonious King	Y	Patricia Holobaugh	Y
	Erin McDowell	Y		
Pre-clinical	La Nissa Brown		Anne Pilaro	Y
Clinical Pharmacology	Mike Staschen	Y		
DMPQ	Mike Vardon	Y	Marion Michaelis	
	Jei He	Y	Destry Sullivan	Y
Epidemiology	Wambui Chege	Y	Manette Nui	Y
DBSQC	Lokesh Bhattacharyya	Y	Lokesh Bhattacharyya	Y
	Hyesuk Kong	Y	Kenney James	
	Josephine Resnick	Y		

#### Additional attendees:

Ginette Michaud, MD, OBRR  
 John A. Eltermann, Jr., RPh, M.S., OCBQ/DMPQ  
 Mahmood Farshid, PhD, OBRR/DH  
 Howard Chazin, MD DHCR/OBRR  
 Iliana Valencia, MS, OBRR

Update (by RPM)

Two inspections were performed by Bimo and DMPQ/CMC  
Information requests were sent (clinical, epidemiology, DMPQ, DBSQC)  
The samples for testing were requested.  
The PNR acceptance letter was issued

Midcycle Meeting Highlights:

- ❖ Major deficiencies were identified
- ❖ There is no need for an Advisory Committee
- ❖ Late Cycle meeting is scheduled on 18-Feb-15

## Brief Summary

### **Colonious King (BIMO)**

Bioresearch Monitoring issued three clinical investigator inspection assignments for two protocols in support of this application. All three inspections have been completed and one Establishment Inspection Report (EIR) is pending receipt. We are currently in the process of reviewing two EIRs and will update the review committee as soon as the review process is complete.

### **Andrey Sarafanov, PhD (CMC)**

Substantive issue was identified by CMC reviewers

- Not validated assay (b) (4) used for DP specification (b) (4) (Section 3.2.P Drug Product (powder))

An IR for less critical or minor issues will be submitted to Octapharma shortly.

### **Nancy Kirchbuan , PhD (CMC)**

During the pre-license inspection of Octapharma AB (October 21 – 28, 2014), the following was observed:

“Control of analytical method R7026-02-01: (b) (4) for analysis of human cell line recombinant Human factor VIII (Human-cl rhFVIII)’ is inadequate in that the method does not perform consistently, as validated during routine control of manufacture...”

### **Peng Ze, PhD (CMC)**

To support the inactivation of (b) (4) by the S/D treatment step in the manufacture of recombinant FVIII, B-domain deleted, please consider modifying the (b) (4) of S/D treatment. This modification should be revalidated.

### **Micheal Varden (DMPQ)**

The issues were listed in the 483 observations issued to the Octapharma Stockholm facility on October 28, 2014. The firm submitted the timeline to respond the issues.

### **Min Lin PhD (Biostatistics)**

No major statistical issues have been identified;

**Carl-Michael Staschen MD (Pharmacology)**

No major issues have been identified. Overall, the study designs for the pharmacokinetic evaluations were adequate and the general conclusions drawn by the sponsor based on the PK assessments in the PK studies are acceptable.

**Loan Nguyen, PharmD (APLB)**

Labeling review has not started yet

**Josephine Resnick(DBSOC)**

Samples for testing are requested. A lot release protocol will not be required.

**Lokesh Bhattacharyya PhD (DBSOC)**

All information requests submitted to-date were addressed. Two new information requests will be submitted shortly.

**Hyesuk Kong (DBSOC)**

No substantive issue at this time.

**Wambui Chege MD (OBE)**

At this time DE/OBE agrees with the postmarketing surveillance and post-approval studies proposed by the sponsor in the Pharmacovigilance Plan (PVP). The 4 proposed postmarketing commitment studies (PMCs) listed in the PVP may prove useful, particularly with regard to current areas of limited information regarding use of the product in specific populations. These studies may be considered clinical PMCs, meaning that should the product be licensed, the studies can be listed as formal commitments on the approval letter and that the sponsor commits to meeting the pre-specified milestones including prompt submission of interim and final study reports to FDA as described in the study timeline. At this time, the available safety data do not substantiate a need for a post-marketing requirement (PMR) study or a Risk Evaluation and Mitigation Strategy (REMS).

END