

## Mid-Cycle Communication Telecon

**Application type and number:** STN 125555/0  
**Product name:** Antihemophilic Factor (Recombinant)  
**Proposed Indication:** The control and prevention of bleeding episodes (also during and after surgery) in adults and children with hemophilia A  
**Applicant:** OCTAPHARMA  
**Meeting date & time:** December 1, 2014, 12:00 to 12:20 pm  
**Committee Chair:** Andrey Sarafanov, PhD  
**RPM:** Jiahua Qian, PhD

### **FDA Attendees:**

Timothy Lee, PhD, Acting Branch Chief, LCH, DHRR, OBRR, CBER  
Andrey Sarafanov, PhD, LCH, DHRR, OBRR, CBER  
Jiahua Qian, PhD, OBRR, CBER  
Christopher Sese, Eastern Research Group

### **OCTAPHARMA Attendees**

Josef Weinberger, Corporate Quality and Compliance Officer  
Olaf Walter, Senior VP International Business Units  
Sigurd Knaub, Vice President Clinical R&D Haematology  
Alex Scheepers, General Manager Octapharma AB  
Christina Leo, Head of Production Unit  
Irena Knappik, Project Manager rFVIII  
Karin Stackerud, Head of Biopharmaceutical Production  
Stefan Ernback, QP Biopharmaceutical  
Ann-Christine Eskekärr, Head of QC Laboratory  
Didier Elmlinger, Head of Corporate Quality Control  
Charlotte Flodin, QA-Manager  
Maya Tiemeyer, Scientific Head Octapharma Biopharmaceuticals  
Ulrich Thibaut, Board Member  
Jürgen Römisch, Senior Vice President R&D Plasma  
Silvio Wuschko, Director of Pharmacology and Toxicology  
Stanley Ammons, Senior Director, Compliance & Government Policy  
Barbara Rangetiner, Director Int. Drug Regulatory Affairs  
Melanie Six, Manager Int. Drug Regulatory Affairs

*Mid-cycle discussion summary was emailed to the firm prior to the telecon, on November 23, 2014*

### **Discussion Summary:**

1. Any significant issues/major deficiencies identified by the review committee to date.  
State during the telecon if there are no significant issues/major deficiencies identified at this time and document the statement in the telecon summary

1. During the pre-license inspection of Octapharma AB in Stockholm (October 21-28, 2014), we observed that the analytical method R7026-02-01 “(b) (4) for analysis of human cell line recombinant Human factor VIII (Human-cl rhFVIII) (b) (4) does not perform consistently. At the same time and as a result of the inconsistent performance of this method, our reviewers encountered problems evaluating the results for (b) (4) in both product release and stability testing as described in Section 3.2.P.8. Thus, this deficiency has hampered the review of product quality and stability data to support the proposed shelf-life of the final drug product. We are proposing a follow-up telecon to ensure that your approach to correct this deficiency will provide the necessary information to satisfactorily address the deficiency within the timeline of the review.
2. We have also identified deficiencies in your viral validation studies. Briefly, they are related to (a) the effectiveness of the solvent/detergent treatment step in inactivating (b) (4); (b) the global log reduction factors for (b) (4) by the 20N nanofiltration step. The details of our comments will be included in an information request (IR).

The above mentioned information request will be sent to the firm this week.

The above mentioned teleconference will be scheduled within next 2 to 3 weeks.

**2. Information regarding major safety concerns. State during the telecon if there are no major safety concerns identified at this time and document the statement in the telecon summary**

At this time, review of the clinical data has not identified any major safety concerns.

**3. Preliminary review committee thinking regarding risk management**

Since the review of the clinical data has not identified any major safety concerns, the review committee does not think that a *Risk Evaluation and Mitigation Strategy* is required.

**4. Any information requests sent and not received**

Information Requested	Expected Response Date
DBSQC IR Dated 3-Nov-14	30-Dec-14
DBSQC IR Dated 20-Nov-14	4-Dec-14
Samples for in-support testing dated 13-Nov-14	Noticed FDA that samples were shipped out today, 1-Dec-2014
Statistical IR Dated 19-Nov-14	8-Dec-14

**5. Any new information requests to be communicated**

Additional IRs will be conveyed to Octapharma soon.

**6. Proposed date for the late-cycle meeting**

The late-cycle meeting is tentatively scheduled on February 18, 2015, but is subject to change depending on the timing and review of the responses to 483 observations and IRs. In addition, please note that if the responses contain a substantial amount of new data or information not previously submitted to, or reviewed by, the agency, the submission could be classified as a major amendment and the goal date will be extended by 3 months.

**7. Updates regarding plans for the AC meeting**

STN 125555/0 will not be presented before the Blood Products Advisory Committee.

**8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates**

None

END