T 910.16: FILING MEETING AGENDA/SUMMARY

Application type and number:	BLA 125612/0
Product name:	Human Fibrinogen
[Proposed indication]:	For the treatment of acute bleeding episodes (b) (4) [redacted] in adult and pediatric patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia
[Applicant]:	Octapharma Pharmazeutika Produktionsges.m.b.H
Meeting date & time:	July 27, 2016 1:00 pm – 2:00 pm
Meeting Chair:	Ze Peng, PhD
Meeting Recorder:	Lorraine Wood, MS, MLS(ASCP)
Background:	This product is a human plasma-derived, sterile, purified, solvent/detergent treated, and nanofiltered fibrinogen concentrate. It is indicated for the treatment of acute bleeding episodes (b) (4) [redacted] in adult and pediatric patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. This product will be available in lyophilized form for intravenous administration after reconstitution.

Table 1: Review Committee and Discipline Filing Decision Summary

Discipline/Organization	Name [with credentials (not title)]	Attended meeting	Fileable	RTF	Deficiencies Identified
Regulatory Project Manager (RPM)	Lorraine Wood, MS, MLS(ASCP)^{CM}	Y	X		
Chair & CMC Product Reviewer	Ze Peng, PhD	Y	X		
Clinical Reviewer	Victor Baum, MD	Y	X		
Clinical Pharmacology Reviewer	Iftekhar Mahmood, PhD	N	X		
Non-clinical Pharmacology & Toxicology Reviewer	Yolanda Branch, PhD	Y	X		
OCBQ/DMPQ Reviewer	Randa Melhem, PhD	Y	X		X
OCBQ/DMPQ/PRB Reviewer	Jacqueline Glen	N			
OCBQ/APLB Reviewer	Kristine Khuc, PharmD	N	X		
OCBQ/BIMO Reviewer	Anthony Hawkins	Y	X		
OCBQ/DBSQC Regulartory Coordinator	Karen Compbell	Y	X		
OCBQ/DBSQC Reviewer	Tao Pan, PhD Grainne Tobin Obinna Echeozo	N Y Y	X X X		
Statistical Reviewer of non-clinical data	Shuya (Joshua) Lu, PhD	Y	X		

Discipline/Organization	Name [with credentials (not title)]	Attended meeting	Fileable	RTF	Deficiencies Identified
and clinical data					
Postmarketing Safety Epidemiological/Pharmacologovigilance Reviewer	Faith Barash, MD, MPH	N	X		
Consult Reviewer(s)	Pending				
Other Attendee(s) OBRR/DHRR/LH Acting Branch Chief OBRR/DHRR OBRR/DHCR/HPRB Branch Chief OBE Team Leader OBRR/RPMS Branch Chief OBRR/DHRR Division Deputy Director OBRR Associated Deputy Director for Science	 Timothy Lee, PhD Michael Kennedy, PhD Mitchell Frost, MD Renee Rees, PhD Iliana Valencia, MS Mahmood Farshid, PhD Mark Weinstein, PhD				

REGULATORY CONCLUSIONS / DEFICIENCIES

1. **Does the application, on its face, appear to be suitable for filing or is the application unsuitable for filing and will require a RTF letter?** *The review committee recommended that this application can be filed.*

2. **If fileable, list any substantive deficiencies or issues that have significant impact on the ability to complete the review or approve the application**:
No substantive review issues have been identified at this time. One deficiency below will be addressed in the filing letter:

While conducting the filing review, the review committee concluded that the human fibrinogen drug product, which will be co-packaged with a transfer device and filter, is a combination product and needs to be in compliance with the following regulations: Management Responsibility (820.20), Design Controls (820.30), Purchasing Controls (820.50), and Corrective and Preventive Action (820.100) as specified in 21 CFR 4.4. The review committee will ask Octapharma to submit as an amendment to this BLA by September 2, 2016, information to demonstrate compliance with the above mentioned regulations, which should also include information on the design of the current device, design history, design verification studies, and all Human Factor studies.

FILING MEETING DISCUSSION, IF FILED:

3. **Indicate any comments on the status of the proprietary name review.**
Proprietary name review was completed on July 19, 2016. ***Update:*** *Proprietary name acceptance letter was submitted to Octapharma on September 2, 2016.*

4. **Indicate whether the product sh/would be subject to lot release, surveillance, or exempt from lot release.** *This product would be subject to lot release.*

5. **What is the review classification of this application?**
The application is under a standard review classification, and has a 12-month review timeline.

6. **Indicate the decision regarding the need for an Advisory Committee.**
No Advisory Committee is needed for this application.

7. **Indicate whether the submission triggers PREA; if yes, a PeRC meeting is needed.**
This application does trigger PREA. Arequest for a deferral was submitted by the applicant in amendment 3 (July 13, 2016) requesting deferral for ages 0 to 2 years, 2 to 5 years and 6 to 12 years. The PeRC meeting is scheduled for December 7, 2016.

8. **Is a comprehensive and readily located list of all clinical sites included or referenced in the application?**
Information requests were sent to Octapharma on July 7, 2016 and July 11, 2016 for additional information regarding the complete street address and contact telephone number for each of the Protocol FORMA-01 and FORMA-02 clinical investigators, respectively. Octapharma submitted this information to the FDA on July 14, 2016, which was found to be acceptable. No additional issues need to be addressed to date regarding listings of clinical sites referenced in the application.

9. **Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?** *Yes.*

10. **Indicate any updates since the first committee meeting on pre-license inspection, pre-approval inspection, or BIMO sites requiring inspections (Is the establishment(s) ready for inspection?)** *The inspection for manufacturing facilities is recommended to be waived.*

The clinical sites identified for BIMO inspection are located in India and the United Kingdom. BIMO is planning to review any available European Medicines Agency (EMA) inspection *reports corresponding to clinical sites the BLA Committee selected for inspection. BIMO submitted a corresponding request through CBER's international affairs advisor on July 19, 2016 to take part in the agency's International Information Sharing pilot with EMA).*

11. **If the application is affected by the Application Integrity Policy (AIP), has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?** *N/A.*

12. **Is the product an Original Biological Product or a New Molecular Entity (NME), for NDAs only?** *No.*

FOR APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs), IF FILED

13. **Confirm that any late submission components were submitted within 30 days. List any late submission components that arrived after 30 days.** *None.*

14. **Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?**
    All reviewers consider the application to be complete for their respective discipline.

ADMINISTRATIVE DETAILS, IF FILED:

15. **Review the Milestone Schedule and indicate if there are any issues with the schedule. Note: This is a confirmation to capture any changes made since the first committee meeting.**
    There are no issues with the milestone and review schedule.

16. **Enter the date of the Mid-cycle Meeting, if appropriate (required for NME NDAs/BLAs in "the Program" PDUFA V):**
    The Mid-cycle meeting is currently scheduled for November 17, 2016 2:30 to 3:30 pm.