Our STN: BL 125612/0

April 13, 2017

Octapharma Pharmazeutika Produktionsges.m.b.H.
Attention: Mr. Stanley Ammons
121 River Street, Suite 1201
Hoboken, NJ 07030

Dear Mr. Ammons:

Attached is a copy of the memorandum summarizing your March 15, 2017 Late-Cycle Meeting with CBER. This memorandum constitutes the official record of the meeting. If your understanding of the meeting outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER in writing as soon as possible.

Please include a reference to STN BL 125612/0 in future submissions related to the subject product.

If you have any questions, please contact LCDR Thomas J. Maruna, USPHS, MSc, MLS(ASCP, CPH at (240) 402-8454 or thomas.maruna@fda.hhs.gov.

Sincerely,

Basil Golding, MD
Director
Division of Plasma Protein Therapies
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research

Late-Cycle Meeting Summary

Application Number:	BL 125612/0
Product Name:	Fibrinogen (Human)
Indication:	Treatment of acute bleeding episodes (b) (4) in adult and pediatric patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia
Applicant Name:	Octapharma Pharmazeutika Produktionsges.m.b.H.
Meeting Date and Time:	March 15, 2017, 10:00 am – 11:00 am, ET
Meeting Format:	Teleconference
Meeting Chair:	Ze Peng, PhD
Meeting Recorder:	Thomas J. Maruna, MSc, MLS(ASCP), CPH

FDA ATTENDEES
Anthony Lorenzo, CBER/OCBQ/DMPQ
Basil Golding, MD, CBER/OTAT/DPPT
Becky Robinson, PhD, CBER/OTAT/DCEPT
Bindu George, MD, CBER/OTAT/DCEPT
Faith Barash, MD, CBER/OBE/DE
Grainne Tobin, PhD, CBER/OCBQ/DBSQC
Karen Campbell, CBER/OCBQ/DBSQC
Kimberly Benton, PhD, CBER/OTAT
Lokesh Bhattacharyya, PhD, CBER/OCBQ/DBSQC
Mahmood Farshid, PhD, CBER/OTAT/DPPT
Rakhi Dalal, PhD, CDRH/OC/DMQ
Ramani Sista, PhD, CBER/OTAT/DRPM
Randa Melhem, PhD, CBER/OCBQ/DMPQ
Renee Rees, PhD, CBER/OBE/DB
Robert Sokolic, MD, CBER/OTAT/DCEPT
Sapana Patel, PharmD., CDRH/ODE/DAGRID
Shuya Lu, PhD, CBER/OBE/DB
Tao Pan, PhD, CBER/OCBQ/DBSQC
Tejashri Purohit-Sheth, MD, CBER/OTAT/DCEPT
Thomas Maruna, MSc, CBER/OTAT/DRPM
Tim Lee, PhD, CBER/OTAT/DPPT
Varsha Garnepudi, CBER/OCBQ/DBSQC
William McCormick, PhD, CBER/OCBQ/DBSQC
Wilson Bryan, MD, CBER/OTAT
Ze Peng, PhD, CBER/OTAT/DPPT

APPLICANT ATTENDEES
Barbara Rangetiner, Director, Int. Drug Regulatory Affairs/General Manager
Juliane Mayerhofer, Int. Drug Regulatory Affairs Manager
Harald Mayer, Head of Operations Support
Cristina Solomon, Senior Director, Clinical R&D
Oliver Hegener, VP, Head of IBU Critical Care
Andrea Jungmann, Deputy Head of cQC Method Validation
Werner Giefing, Head of Quality Assurance
Stanley Ammons, Senior Director, Compliance & Government Policy
Karl Leitner, Plant Manager
Ernst Metzger, Head of Corporate Pilot Production
Martina Schwarz, Head of cQC Method Validation
Bruce Schwartz, Director, Clinical R&D
Olaf Walter, Board Member
Wolfgang Frenzel, International Medical Director

BACKGROUND
BLA 125612/0 was submitted on June 9, 2016 for Fibrinogen (Human).

Proposed indication: Treatment of acute bleeding episodes (b) (4) in adult and pediatric patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia

PDUFA goal date: June 9, 2017

In preparation for this meeting, FDA issued the Late-cycle Meeting Materials on February 10, 2017.

DISCUSSION

1. Introductory Comments:

   The Regulatory Project Manager (RPM) noted that the Late-Cycle meeting is prepared by the FDA for all original Biologic License Applications that qualify under the PDUFA V Program, and is intended to provide a status update on the progress of substantive review issues identified to date, and to communicate FDA's objectives for the reminder of the review cycle for original BLA 125612/0. This meeting is not intended to discuss the pending regulatory decision for the application.

   The Review Committee Chair reviewed the following:

   Date of submission: June 9, 2016

   Product: Fibrinogen (Human) [FIBRYNA]

Indication: Treatment of acute bleeding episodes (b) (4)
in adult and pediatric patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

Action date: June 9, 2017

2. Discussion of Substantive Review Issues:

Clinical:
The response to the February 6, 2017, request for additional information was received and no further review issues have been identified to date.

There were no subjects who received the investigational product for treatment of major bleeding. We note the limited number of adolescent subjects but given the rarity of the disease, we may consider the totality of data from pharmacokinetic and hemostatic control in adult subjects with minor bleeding to evaluate efficacy in the adolescent subjects.

(b) (4)

FDA noted that the Case Report Forms may need to be reassessed for quality prior to any future submissions to us for review.

Device/Combination Product:
The response to the February 6, 2017, request for additional information was received and is under review. Additional outstanding information is expected to be received March 20, 2017.

The sponsor had stated testing was conducted according to ISO 7886. However, it was not clear if the testing was performed in accordance with the standard that is related to sterile hypodermic syringes. The sponsor was asked to include in the test report how the standard is related to their device.

FDA reminded Octapharma to submit the completed test reports for all tests on the device constituent.

FDA informed Octapharma that the responses to the sterility and biocompatibility IRs are currently under review.

Two additional requests for additional information will be prepared and issued.

3. Additional Applicant Data:

   Clinical:
   Octapharma noted that recruitment has been an issue, particularly for surgical subjects.

   Octapharma acknowledged FDA's request to reassess the quality of the CRFs submitted.

4. Postmarketing Requirements (PMR)/Postmarketing Commitments (PMC):

   A decision regarding PMR and PMC studies is under internal discussion and will be communicated shortly.

   In lieu of a post-marketing commitment for the essential performance requirements of the co-packaged combination product, stability data to support the essential performance requirements of the device constituent at the end of shelf-life would be considered acceptable.

5. Major Labeling Issues:

   Labeling negotiation will occur later in the review cycle; as early as April and May 2017.

6. Application Questions:

   Octapharma requested clarification concerning possible outcomes should they fail to submit all requested information. FDA reminded Octapharma that the regulatory decision would not be discussed at this meeting; a final decision will be made on the action due date for the file. Octapharma should be aware that if the amendments are determined to contain substantive and/or previously un-reviewed data at any time during the review cycle, these amendments may be designated as major and extend the review clock by 3 additional months.

7. Wrap-up and Action Items:

   Additional requests for information will be sent to Octapharma in relation to the proposed device/combination product.

This application has not yet been fully reviewed by the signatory authorities, Division Directors and Review Committee Chair and therefore, this meeting did not address the final regulatory decision for the application.

END