From: Maruna, Thomas
Sent: Thursday, March 23, 2017 3:21 PM
To: 'Ammons, Stanley'
Cc: Peng, Ze; Dalal, Rakhi; Mayerhofer, Juliane (juliane.mayerhofer@octapharma.com)
Subject: 23-Mar-2017 Information Request - BLA 125612.0 - Response due 30-Mar-2017

Importance: High

STN: BL 125612/0
BLA INFORMATION REQUEST

Octapharma Pharmazeutika Produktionsges.m.b.H.
Attention: Mr. Stanley Ammons
March 23, 2017
Sent by email

Dear Mr. Ammons:

We are reviewing your biologics license application (BLA) dated June 9, 2016, for Fibrinogen Concentrate (Human), and have determined that the following information is necessary to take complete action. Please promptly submit your written response to the following items so that we may continue evaluating your BLA:

1. Per the BLA 125612/ Amendment #0031, Document 125DRS4x, dated 01/20/2017, the "Fibrinogen is .... reconstituted with the dedicated transfer device Octajet using 50 ml water for injection and is filtered prior intravenous application. The use of the drug product Fibrinogen (constituent part 1) together with the reconstitution device Octajet (constituent part 2) and the syringe filter (constituent part 3) is defined as combination product Octafibrin as codified in 21 CFR part 4." In the response to the Agency's Filing Letter dated 08/05/2016 regarding the information on the firm's current Good Manufacturing Practice (cGMP) under the 21 CFR Part 4, limited Design Control (21 CFR 820.30) information is submitted to FDA. Depending on the cGMPs followed under 21 CFR 4.4, summary of the below Quality System information should be submitted for FDA review. Information on how to demonstrate compliance to the 21 CFR Part 4 and the Call-Outs, consider the FDA guidance document, Current Good Manufacturing Practice Requirements for Combination Products, January 2017. For preparation of the summary related to the applicable 21 CFR Part 820 regulations, consider the FDA guidance document "Quality System Information for Certain Premarket Application Reviews; Guidance for Industry and FDA Staff," February, 2003.

    a. Management Responsibility (21 CFR 820.20)

Provide a summary of how your firm has established responsibility to assure that the combination product is manufactured in compliance with applicable 21 CFR Part 4 requirements. Also, provide a description of the functions and responsibility of each facility involved in the manufacturing of the combination product and its constituent parts.

b. Purchasing Controls (21 CFR 820.50)
Provide a summary of the procedure(s) for purchasing controls. The summary should:

i. Describe your supplier evaluation process and describe how it will determine type of and extent of control it will exercise over suppliers.
ii. Define how you maintain records of acceptable suppliers and how you address the purchasing data approval process.
iii. Explain how you will balance purchasing assessment and receiving acceptance to ensure that products and services are acceptable for their intended use.

Explain how the procedure(s) will ensure that changes made by contractors / suppliers will not affect the final combination product. Provide a description of how you applied the purchasing controls to the suppliers/contractors involved in the manufacturing of the combination product or provide evidence of the application (i.e. supplier's agreement).

c. Corrective and Preventive Action (21 CFR 820.100)

Summarize the procedure(s) for your Corrective and Preventive Action (CAPA) System. The CAPA system should require analysis of:

i. Sources of quality data to identify existing and potential causes of nonconforming practices and products;
ii. Investigation of the cause of nonconformities;
iii. Identification of actions needed to correct and prevent recurrence of non-conformances;
iv. Verification or validation of the actions.

2. In BLA 125612/Amendment 35, materials for the (b) (4) components of the Octajet was changed during development of the device. Information in regards to change control for the device is not provided in the BLA. Please provide the procedure for the identification and documentation of the design change and summary of the controls used prior to implementation of a change.

3. Provide the facility information which maintains the design history file for the Octajet and (b) (4) Syringe Filter (b) (4) devices which are secondarily packaged with Fibryna. Please be noted that FDA recognized the dedicated transfer device Octajet device as cross-labelled in BLA 125612.

Please submit your response in a timely manner, as noted below, so we may continue the review of your application. If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

Please submit your responses as an amendment to this file **NO-LATER-THAN March 30, 2017**, referencing the date of this request.

The action due date for these files is June 9, 2016.

If you have any questions, you may contact me directly.

Very Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH
Lieutenant Commander, U.S. Public Health Service
Senior Regulatory Management Officer

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