From:	Maruna, Thomas
Sent:	Tuesday, March 21, 2017 9:56 AM
To:	Ammons, Stanley
Cc:	Mayerhofer, Juliane (juliane.mayerhofer@octapharma.com); Pan, Tao; Peng, Ze
Subject:	21-Mar-2017 Information Request - BLA 125612.0 - Response due 20-Apr-2017

STN: BL 125612/0
BLA INFORMATION REQUEST

Octapharma Pharmazeutika Produktionsges.m.b.H.
Attention: Mr. Stanley Ammons
March 21, 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:

In Amendment 125612/0.36, you provided additional data to address the accuracy of the (b) (4) assay by:

- Analyzing the (b) (4) standards using the (b) (4) method and comparing the measured values with theoretical values; and
- Analyzing (b) (4) standards with (b) (4) and (b) (4) methods, and comparing the measured values by these two methods with the measured values by (b) (4) method.

However, your data do not demonstrate accuracy and specificity of your method because:

- (b) (4) standards were measured against themselves, the effect of the drug product matrix on the accuracy and specificity was not addressed.
- Neither (b) (4) nor (b) (4) method has been validated by the sponsor for the drug product.
- The "correction factors" obtained by measuring a limited number of samples can't be used for the validation of the (b) (4) method.

We fully understand that different proteins have different response factors in different protein assays, which is the reason that a "spike-recovery" study by spiking (b) (4) standard into drug product samples was suggested in our original request. If you prefer to validate the accuracy of (b) (4) method with the result of an orthogonal method, such as (b) (4) method, the orthogonal method should be validated for the drug product;

and second, the drug product should be analyzed to demonstrate comparable results by both methods.

1. Please provide accuracy and specificity data using the drug product as the analyte (and (b) (4) as the standard, if applicable), as requested in our original IR (dated Sept 27, 2016) within 4 weeks from the date of receipt of this request.

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 April 20, 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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