From: Wood, Lorraine
To: Ammons, Stanley
Subject: Information Request for BLA 125612: Analytical Methods
Date: Tuesday, September 27, 2016 10:38:00 AM
Importance: High

Dear Mr. Ammons,

We are reviewing your submission for BLA 125612 and we request the following information to continue our review:

For the method for the determination of the (b) (4) (Document #130SOP184/01: Determination of b) (4) in fibrinogen final containers):

1) Please provide detailed description of the (b) (4) part of the method, including information on the sample preparation (b) (4), and the range of the method, etc.

2) Only the accuracy and precision were validated for this method (Validation report #000VAL184FC347/01: Determination of (b) (4) in fibrinogen FC samples), but as a critical assay for release testing of the drug product, the method needs to be fully validated by assessing its linearity, range, specificity, and robustness within the drug product matrix, in addition to the accuracy and precision. Please provide the requested data.

3) The accuracy of the method was validated by measuring the (b) (4) of an international standard. The accuracy should be evaluated using the drug product, by spiking drug product with known amounts of a standard and determining the recovery (spike recovery). Please provide accuracy data using the spike recovery method.

For method validation of the b) (4) assay (Document #130SOP149/14: Determination of b) (4) by the (b) (4) method):

1) You have evaluated the accuracy of the assay by comparing the assay result of (b) (4) assay after a mathematical correction (Validation report #000VAL149 FC347/00: Determination of b) (4) in fibrinogen final containers by the b) (4) method). The accuracy of the method should be validated within the drug product matrix over the designated range, preferably by spiking different amounts of traceable protein standard such as into drug product, and assessing the recoveries of the spiked proteins over the assay range. Please provide the requested data. If you plan to use the results from an alternate method such as (b) (4) assay, please provide data using the drug product and demonstrate that the results from the (b) (4) methods are comparable without a correction factor.

Please respond to this request by October 25, 2016.

Thank you

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