From:	Wood, Lorraine
To:	Ammons, Stanley
Subject:	Information Request for BLA 125612: Response Requested by December 8, 2016
Date:	Friday, November 18, 2016 4:35:00 PM
Attachments:	image001.png image002.jpg image003.jpg image004.jpg image005.jpg image006.jpg
Importance:	High

Dear Mr. Ammons,

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

We have reviewed your Response to Information Request, in Amendment 12, dated 19 September 2016, for the Determination of Fibrinogen by b) (4) , and have the following Information Requests:

1. We do not agree that your explanation to our IR question # 1.i.a on why different tests produce different results is based on science. In addition, you have not provided any data in support of your explanation. Please provide data as requested in our previous IR.

2. Please provide your Reference Standard qualification protocol and report, including data demonstrating how the qualified potency of your reference standard is determined.

3. We do not agree that comparison of the results obtained by the (b) (4) assay to either the (b) (4) demonstrates method specificity. Please provide adequate data to show your method specificity. We suggest that you analyze the sample matrix (without fibrinogen), to demonstrate negligible activity. Results from a mock but representative sample matrix are acceptable. We also suggest that you provide results of analysis of your product in the presence of a b) (4) at a suitable concentration to show that the assay is specifically inhibited in the presence of the inhibitor to demonstrate specificity of your method.

4. We do not agree with your assessment that b) (4) into drug product is irrelevant since you dilute your drug product with (b) (4) as part of your assay. Therefore we do not agree with your explanation to our previous IR question # 1.ii. Please provide accuracy data as previously requested.

5. You stated that the b) (4) assay was only performed at ODE as an identity test, while the testing at OPG is for b) (4) content; hence it is not necessary to show comparability between the two sites. However, you stated in your Method Comparison Report, 000VAL111 FC 347 348/00 MCR OPG-

ODE/00 that the method comparison was carried out to “prove the comparability of the performance of the validated methods at both laboratories by comparative testing.” The two statements appear to be contradictory. If the statement in your Method Comparison Report is correct, please explain why the results between the two sites are so different. If the statement is not correct, please withdraw this report from your submission.

Please respond to this request by December 8, 2016.

Thank you

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