

From: Do, Yu
To: Joan.robertson@grifols.com
Subject: Information Request (Response Due by Tuesday, February 14, 2017): Original BLA, BL 125640/0, Fibrin Sealant (Human), Instituto Grifols, S.A.
Date: Tuesday, January 31, 2017 3:51:00 PM
Attachments: [image001.png](#)
Importance: High

Dear Ms. Robertson:

We are reviewing your original November 3, 2016, submission to BLA 125640 for Fibrin Sealant (Human). We determined that the following information is necessary to continue our review:

1. Regarding analytical procedure “(b) (4) in Fibrinogen by (b) (4)” (Document No. IG_MA-000158E_ING, Version 7.0):
 - a. Your procedure document instructs, “Prepare the control (b) (4) in the Sections 4.2 and 4.3, respectively. These instructions are too vague. Please define acceptable time durations between (b) (4), sample preparation steps, and sample (b) (4) .”
 - b. For an (b) (4) method, acceptance criteria of system suitability test (SST), such as (b) (4) for (b) (4) performance, should be set as part of the system suitability check. Please revise your analytical procedure document to add these acceptance criteria and submit for review.
 - c. In Section 4.1 on page 5, you describe, “During this (b) (4), perform a fibrinogen product (b) (4) (for instance, fibrinogen control) as part of the (b) (4) .” Is (b) (4) of fibrinogen control sufficient? Please describe the acceptance criterion for (b) (4) .
 - d. You assigned the (b) (4) in the (b) (4) (page 9) as an (b) (4) . Please provide experimental data to support identification of this (b) (4) .
 - e. You described the (b) (4) in the (b) (4) (page 9) as due to an (b) (4) of fibrinogen and not due to (b) (4) . Please provide adequate characterization data to support that this (b) (4) is indeed due to an (b) (4) .
2. Please provide appropriate data to show that no portions of fibrinogen in your product, particularly (b) (4), are (b) (4) under the proposed (b) (4) in the analytical procedure of “(b) (4) in Fibrinogen by (b) (4)” (Document No. IG_MA-000158E_ING, Version 7.0).
3. Regarding “Validation for Fibrinogen (Sealant) of (b) (4) in Fibrinogen by (b) (4)” (Document No. IG_IVMA-000041_ING, Version 2.0):
 - a. Please provide your results to demonstrate the linearity of (b) (4) and (b) (4), either separately or combined, by plotting the (b) (4) against

(b) (4) with the linear regression analyses.

- b. We do not agree with the LOQ determination in your validation report, in which you obtained s and S values for $10s/S$ from the plot of % (experimental (b) (4)) against % (theoretical (b) (4)). You should plot (b) (4) (response) of (b) (4) against its respective (b) (4) (reportable result) to obtain the s (deviation of the (b) (4)) and S (slope of the linear regression) for the calculation. Please recalculate and submit the result for review.
- c. Please provide results of the robustness evaluation of the method.

The review of this submission is ongoing, and issues may be added, expanded upon, or modified as we continue to review this submission. Please submit your response as an amendment to this file by February 14, 2017, referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact the Agency immediately so a new response date can be identified.

If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

The action due date for this file is November 3, 2017.

Please acknowledge receipt of this request and contact me at (240) 402-8343 or Yu.Do@fda.hhs.gov if you have any questions.

Sincerely,

Yu Do, M.S.
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